Figure 1

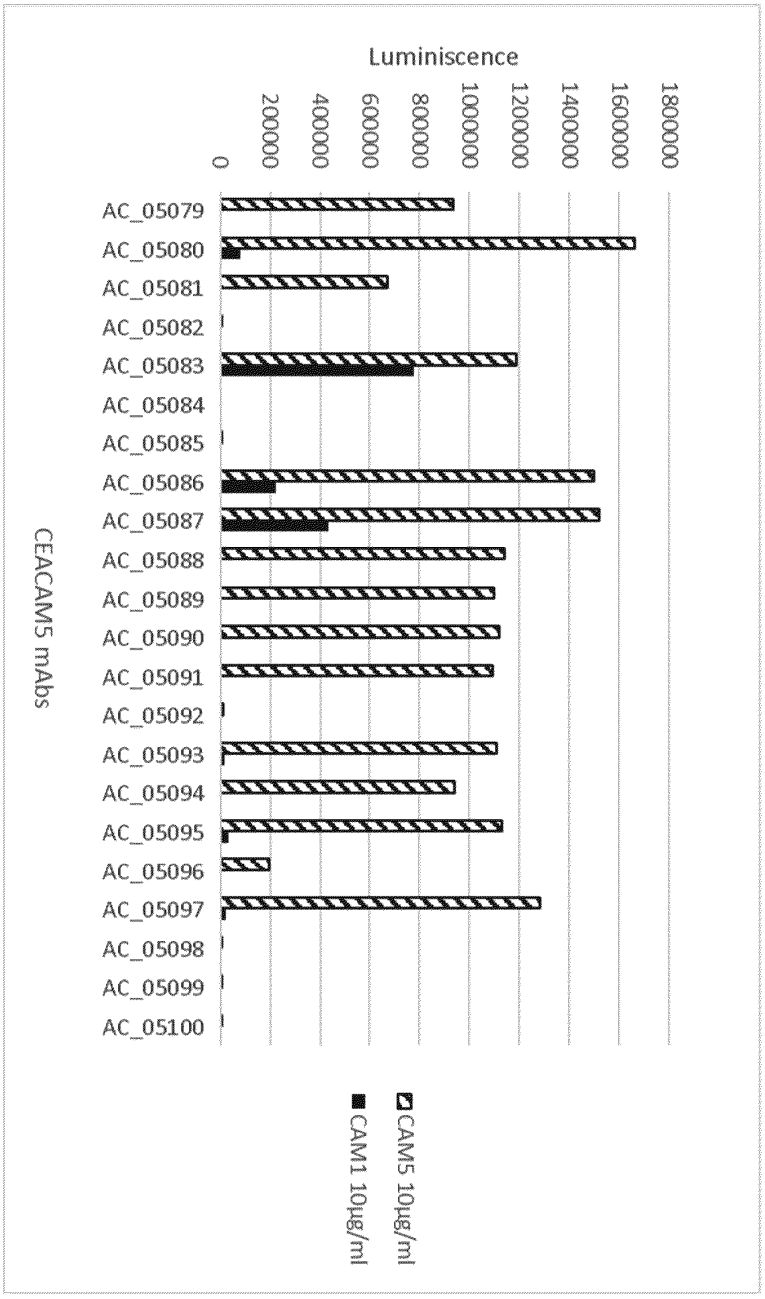

Luminiscence
0
200000
400000
600000
800000
1000000
1200000
1400000
1600000
1800000
AC_05079
AC_05080
AC_05081
AC_05082
AC_05083
AC_05084
AC_05085
AC_05086
AC_05087
AC_05088
AC_05089
AC_05090
AC_05091
AC_05092
AC_05093
AC_05094
AC_05095
AC_05096
AC_05097
AC_05098
AC_05099
AC_05100
CEACAM5 mAbs
CAM1 10µg/ml
CAM5 10µg/ml

Figure 2 (1/2)

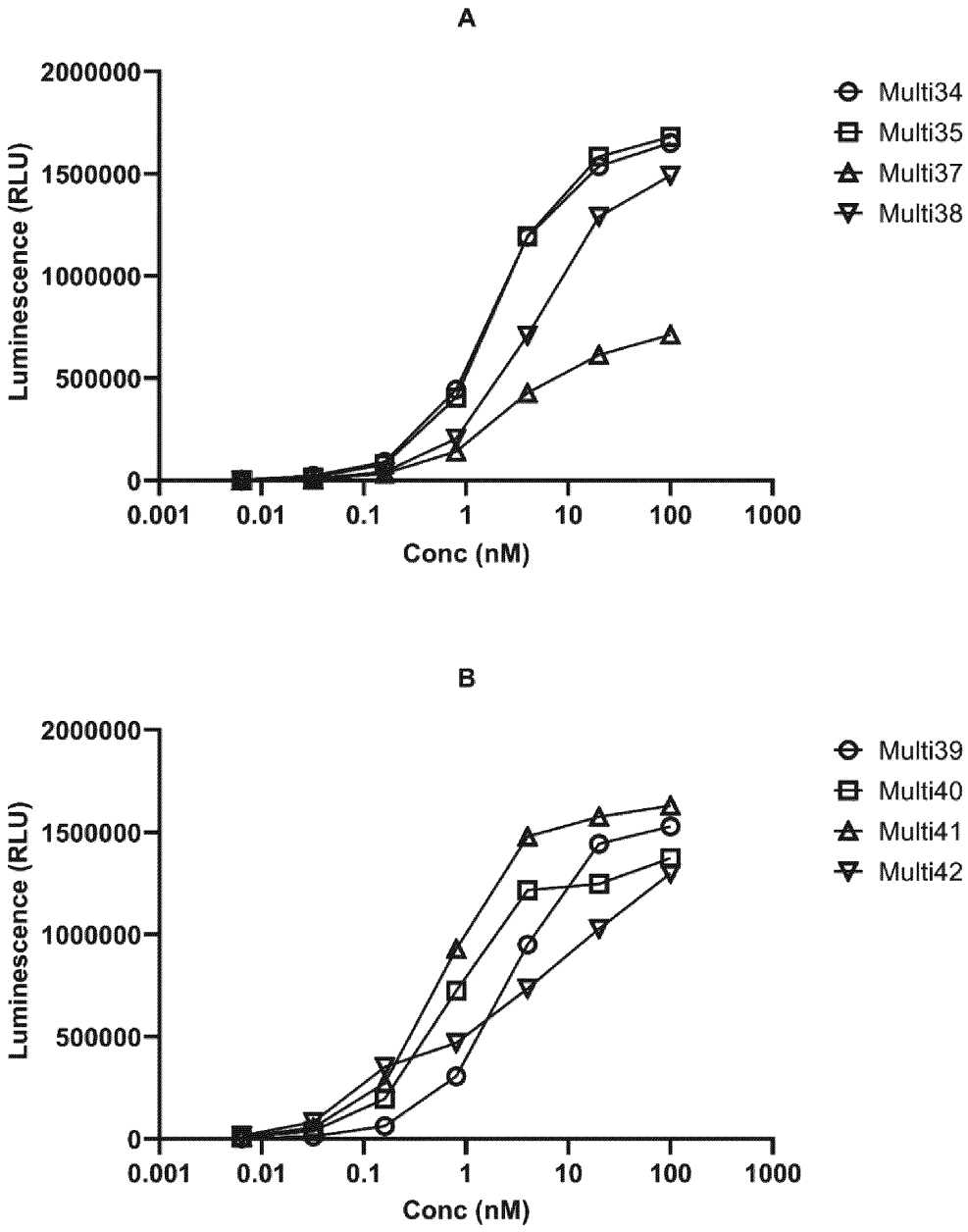
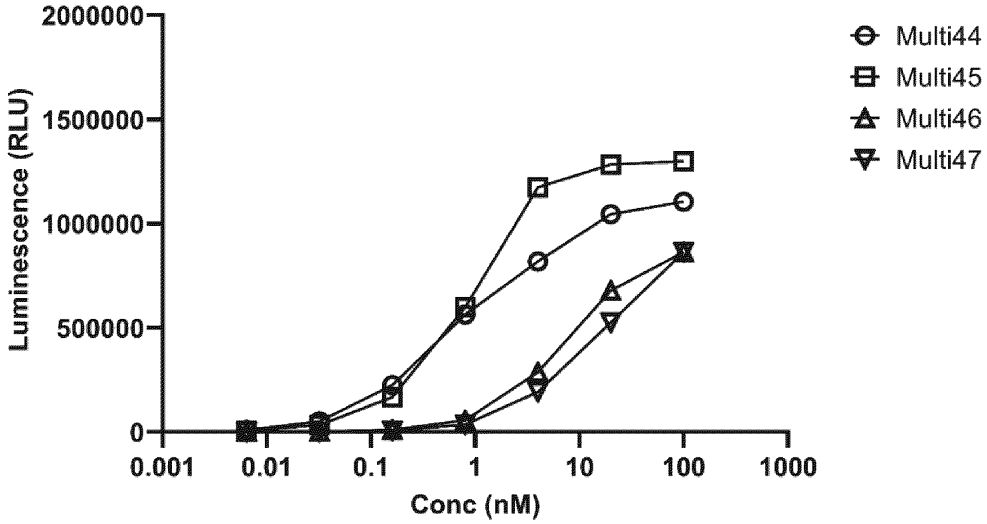

A
2000000
1500000
1000000
500000
0
Luminescence (RLU)
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
Multi34
Multi35
Multi37
Multi38
B
2000000
1500000
1000000
500000
0
Luminescence (RLU)
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
Multi39
Multi40
Multi41
Multi42

Figure 2 (2/2)

C



D

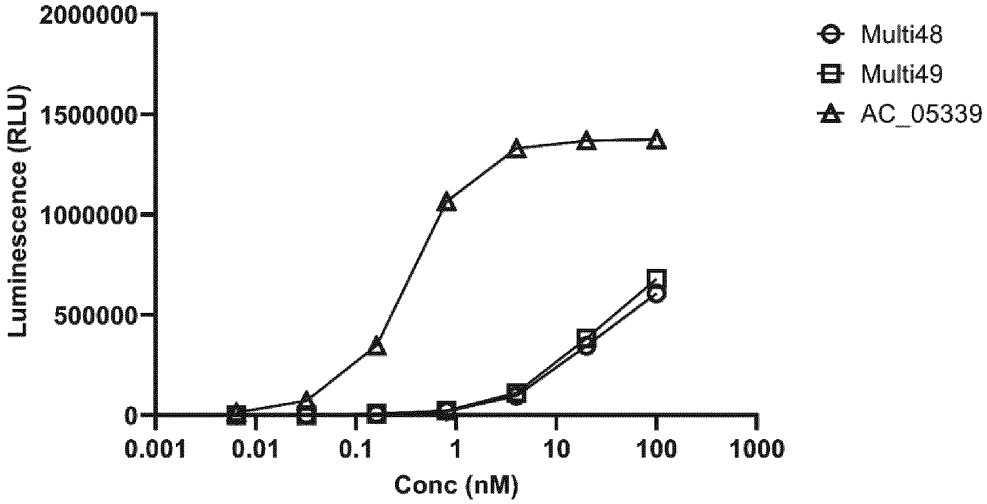


Figure 3 (1/7)

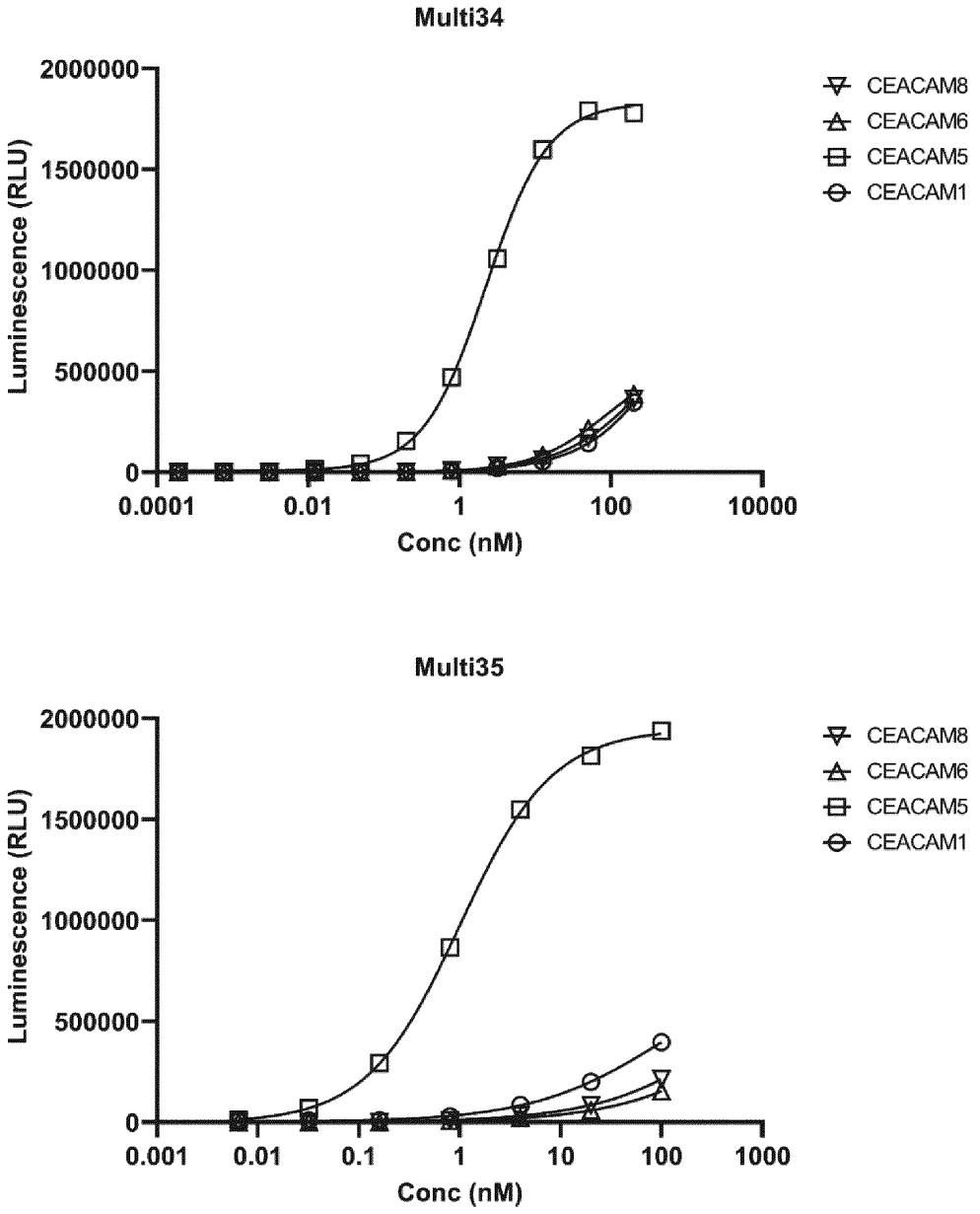

Multi34
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.0001
0.01
1
100
10000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1
Multi35
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1

Figure 3 (2/7)

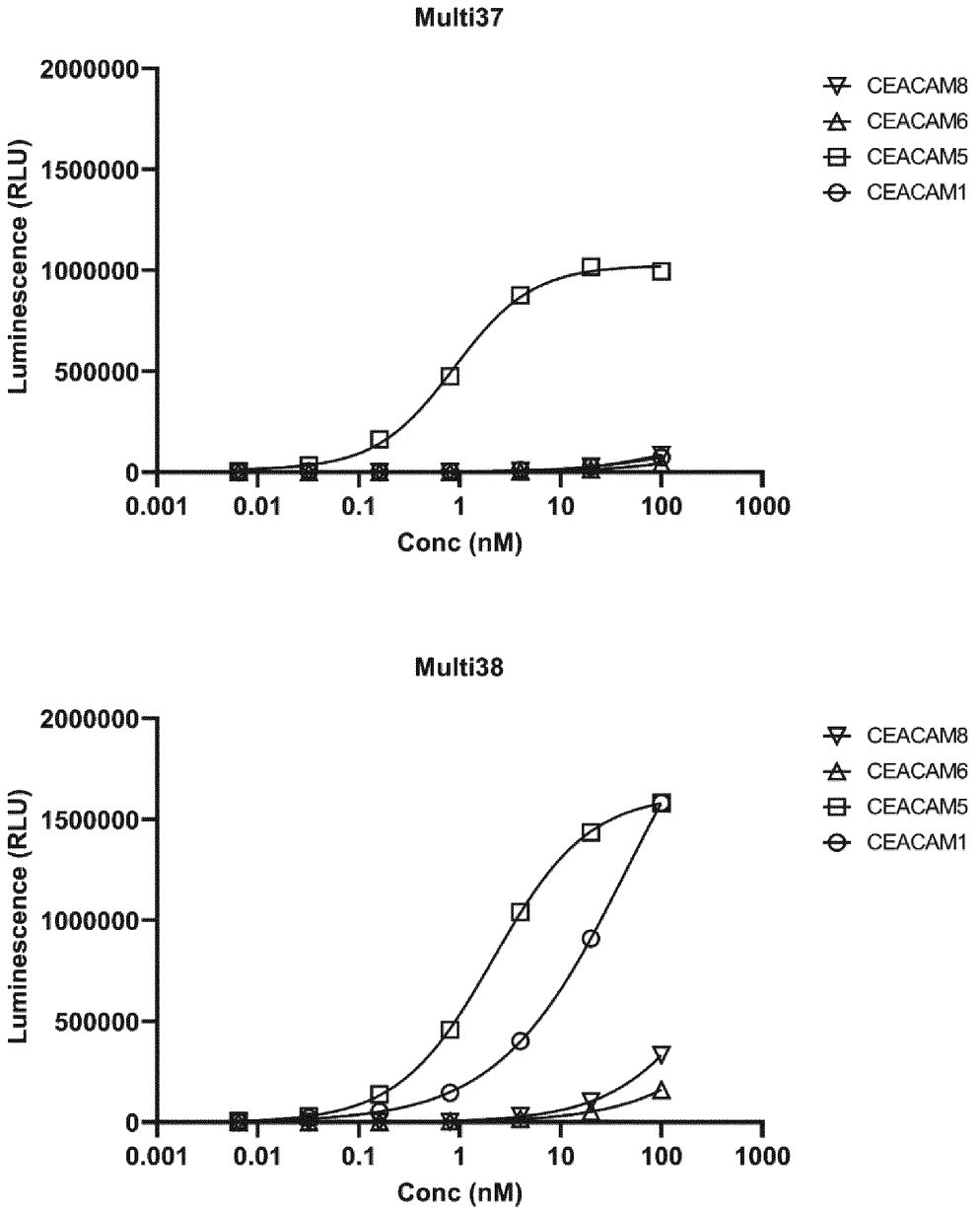

Multi37
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1
Multi38
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1

Figure 3 (3/7)

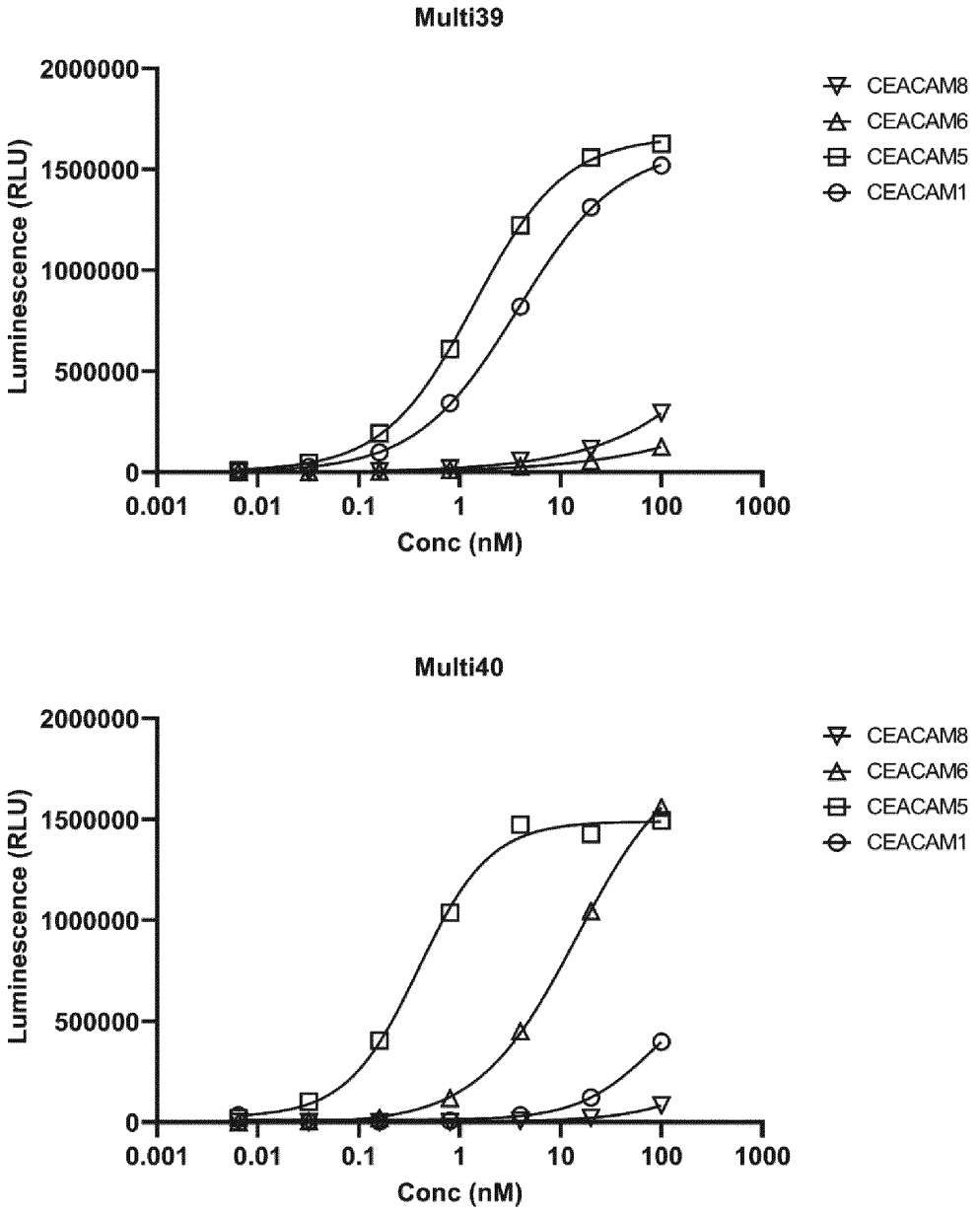

Multi39
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1
Multi40
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1

Figure 3 (4/7)

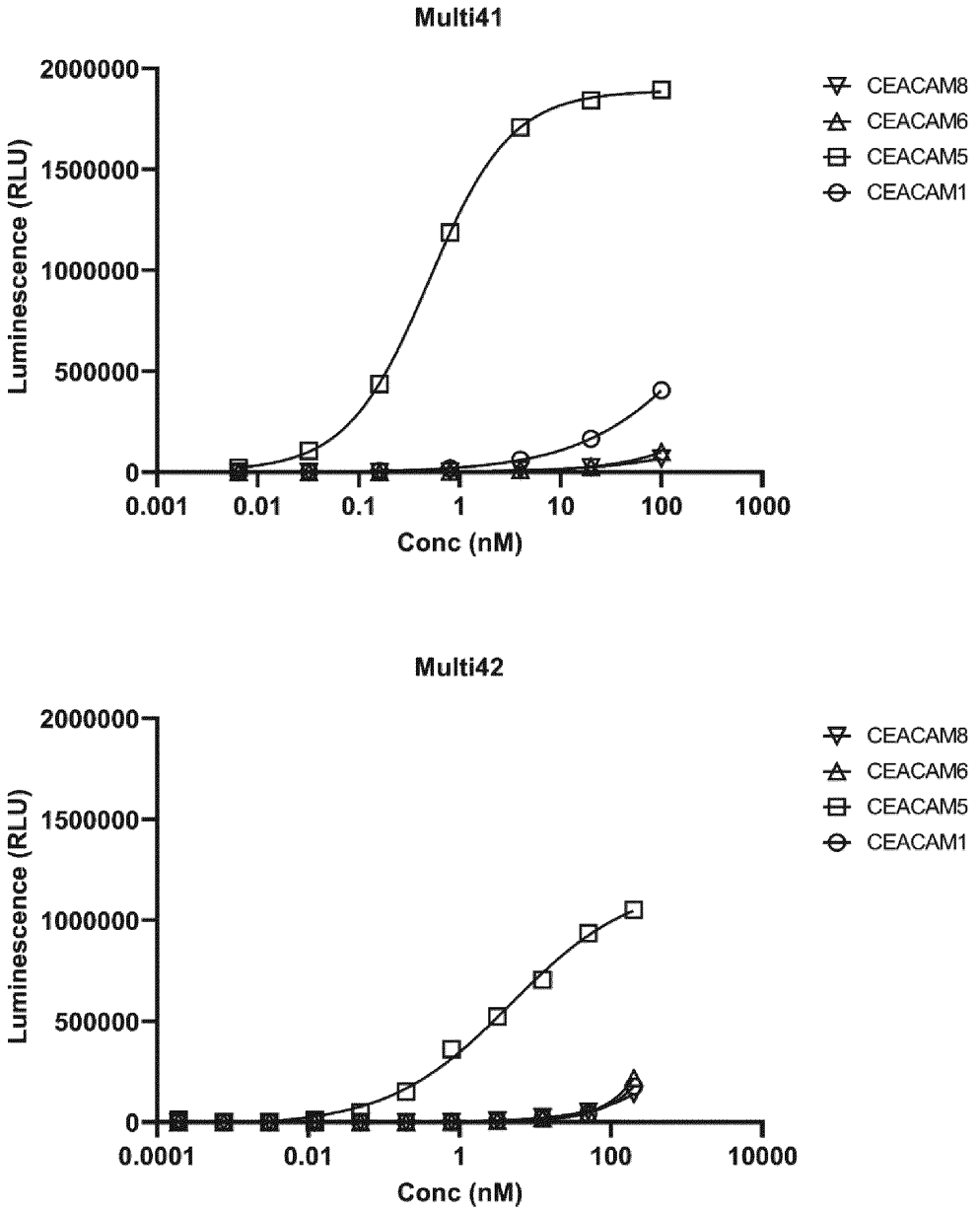

Multi41
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1
Multi42
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.0001
0.01
1
100
10000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1

Figure 3 (5/7)

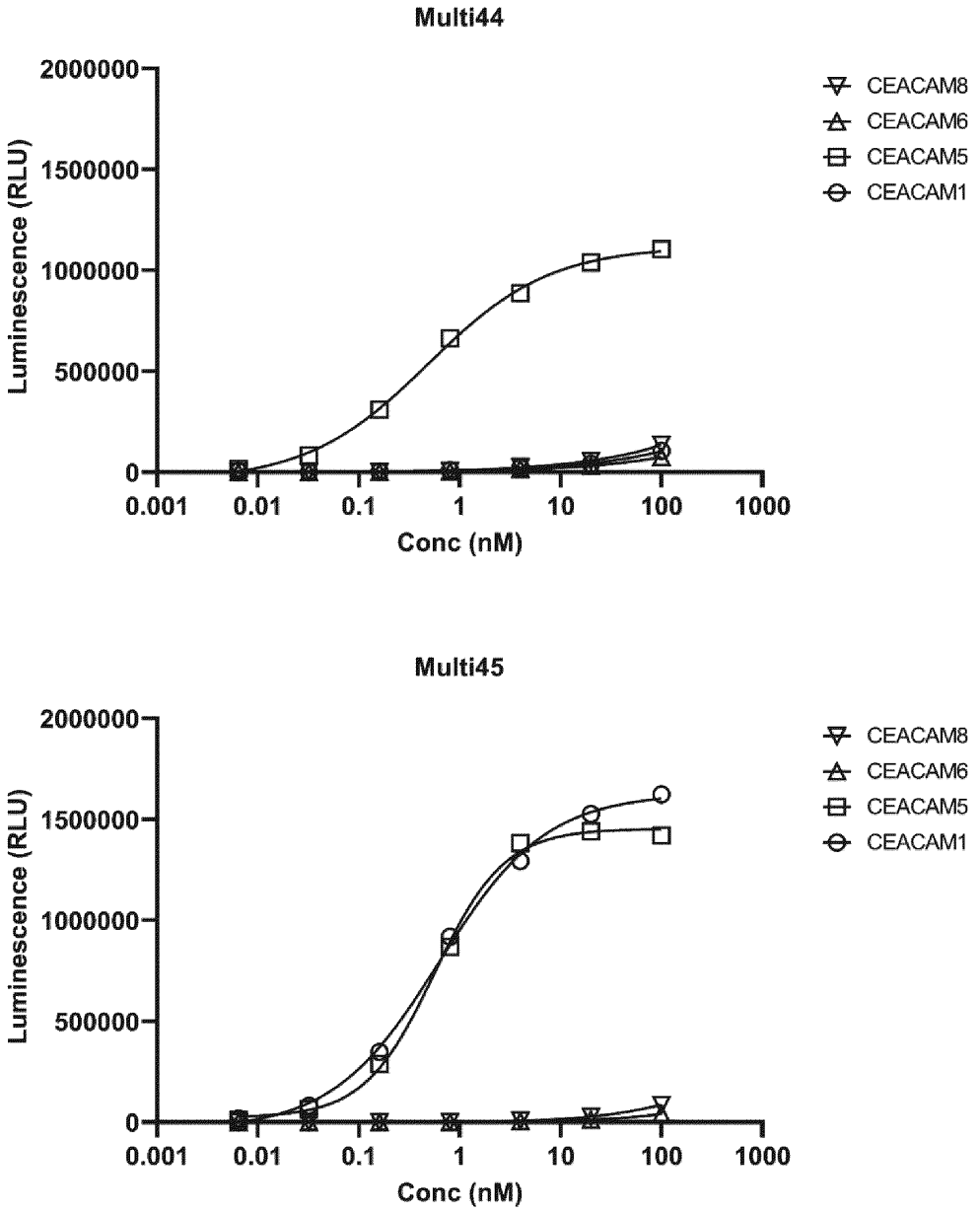

Multi44
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1
Multi45
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1

Figure 3 (6/7)

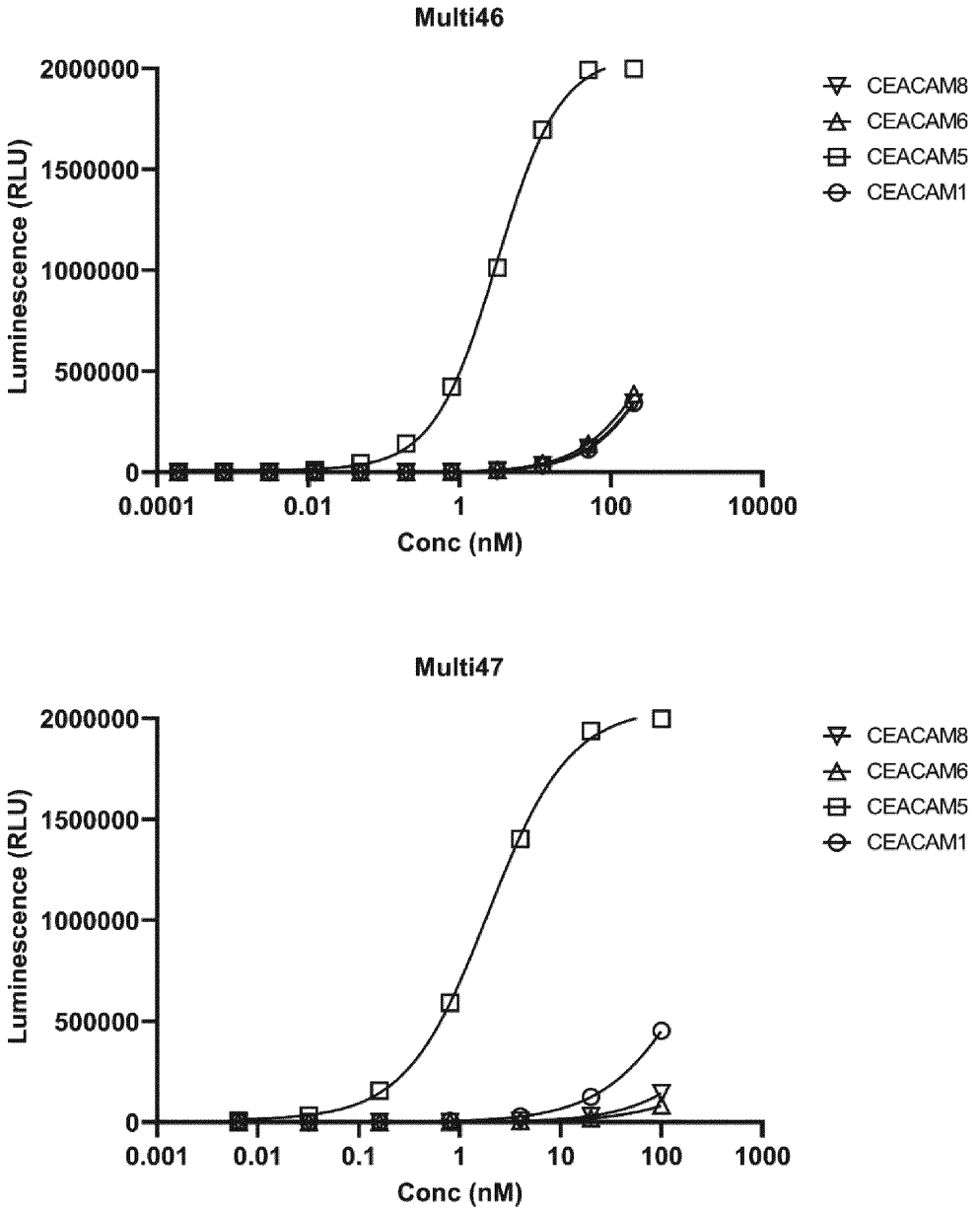

Multi46
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.0001
0.01
1
100
10000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1
Multi47
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1

Figure 3 (7/7)

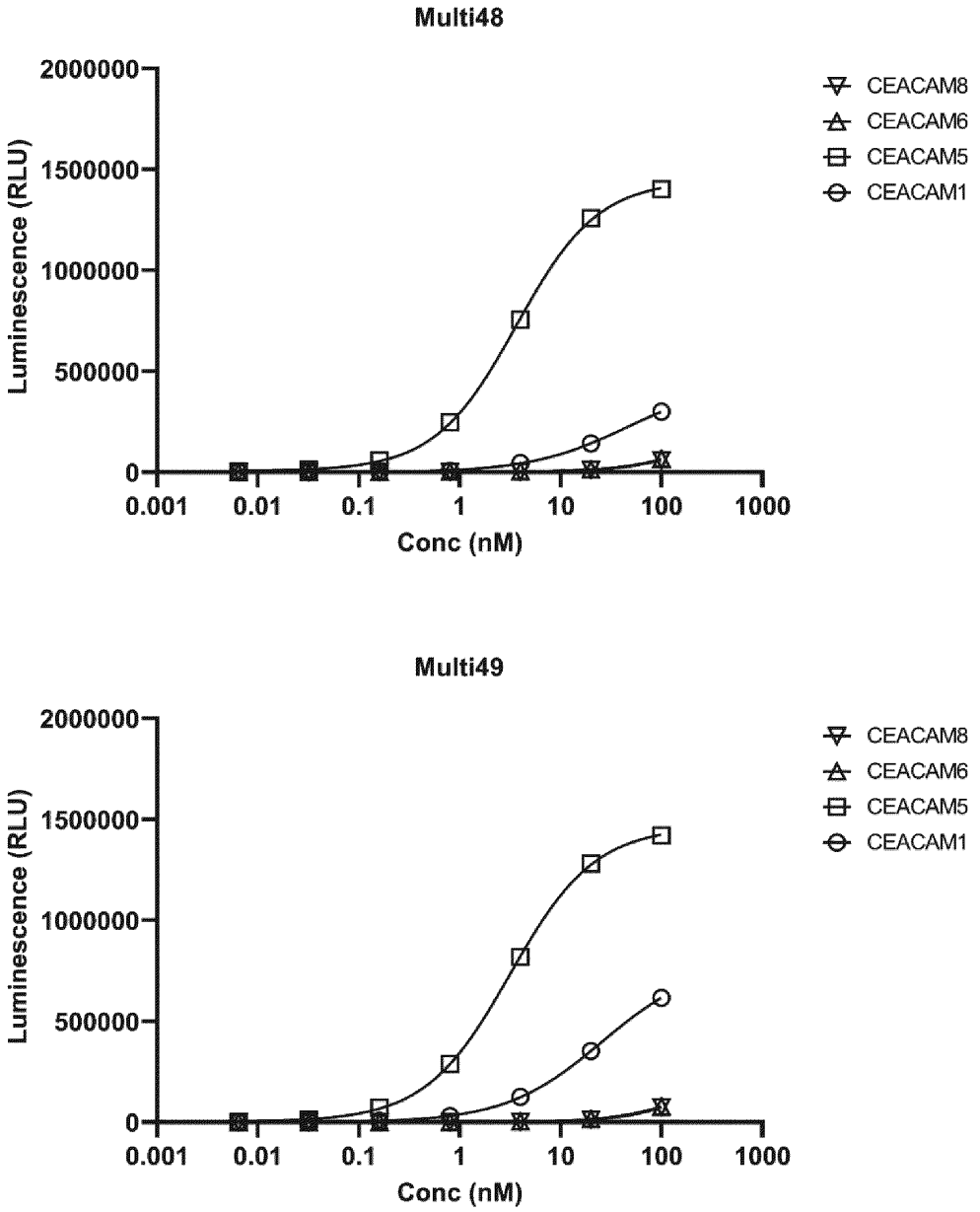

Multi48
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1
Multi49
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.001
0.01
0.1
1
10
100
1000
Conc (nM)
CEACAM8
CEACAM6
CEACAM5
CEACAM1

Figure 4

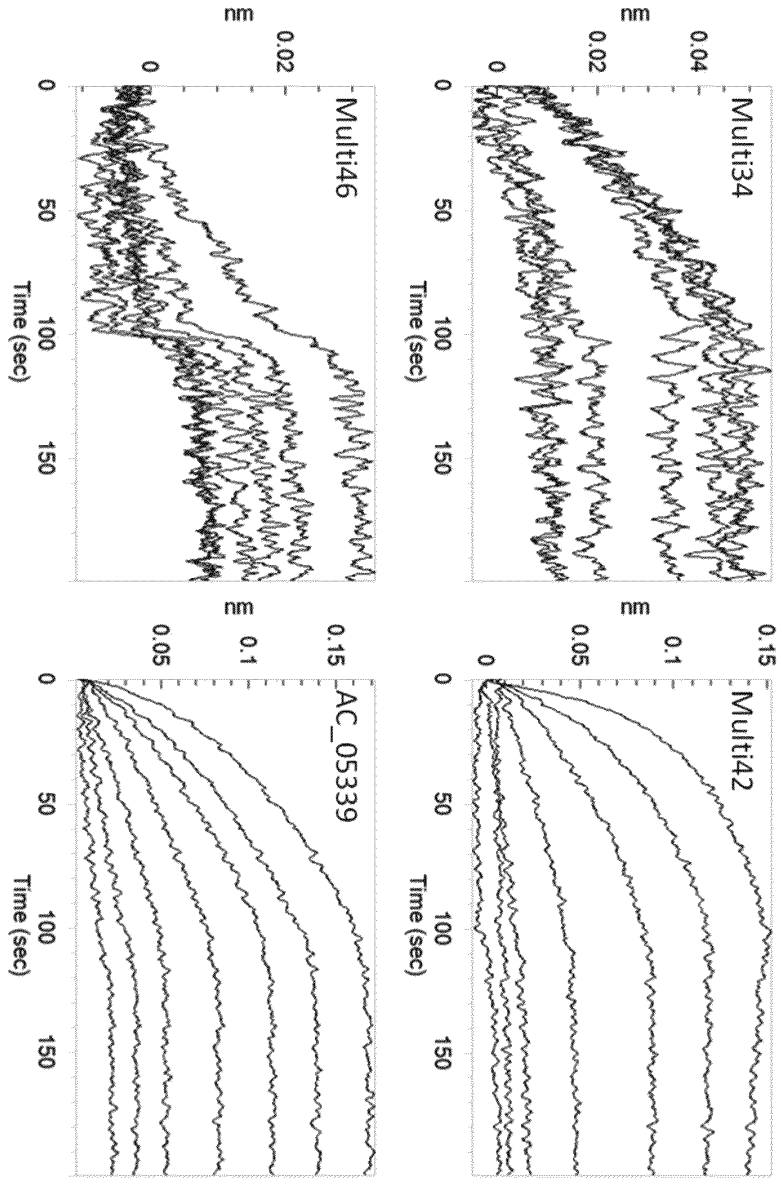

Multi34
Multi46
Multi42
AC_05339
nm
Time (sec)
0
50
100
150
0.02
0.04
0.05
0.1
0.15

Figure 5

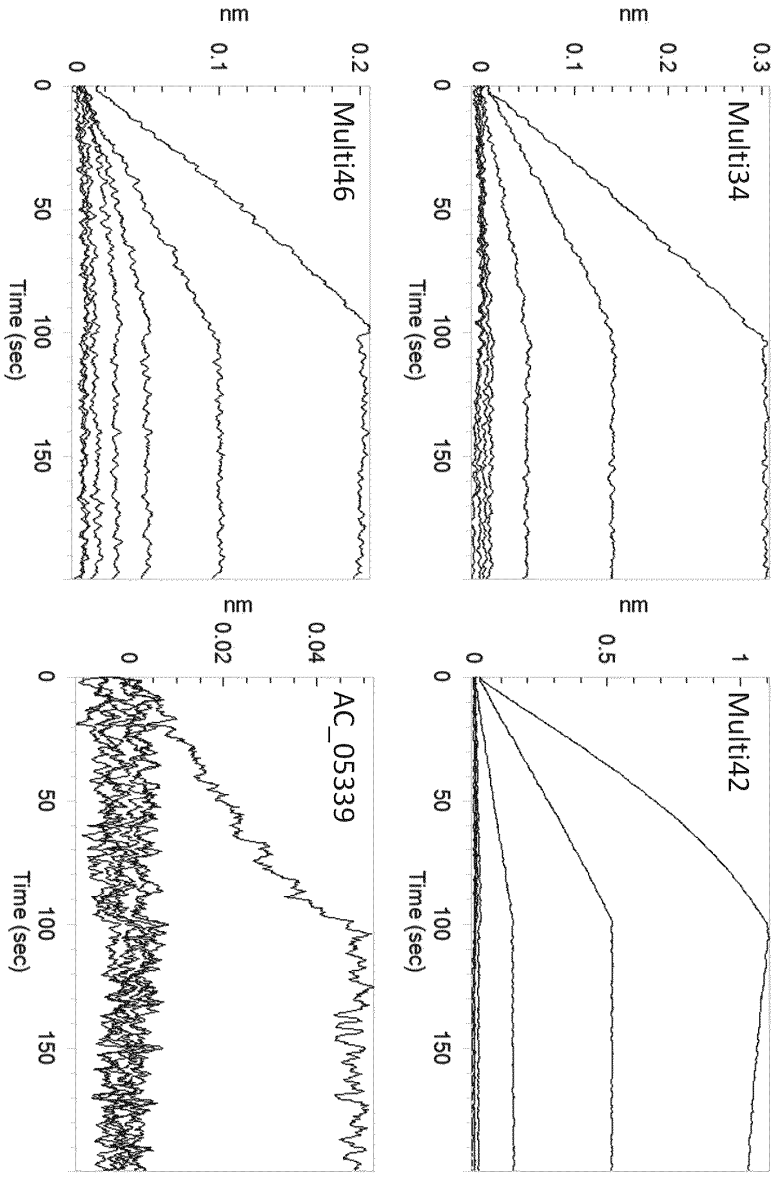
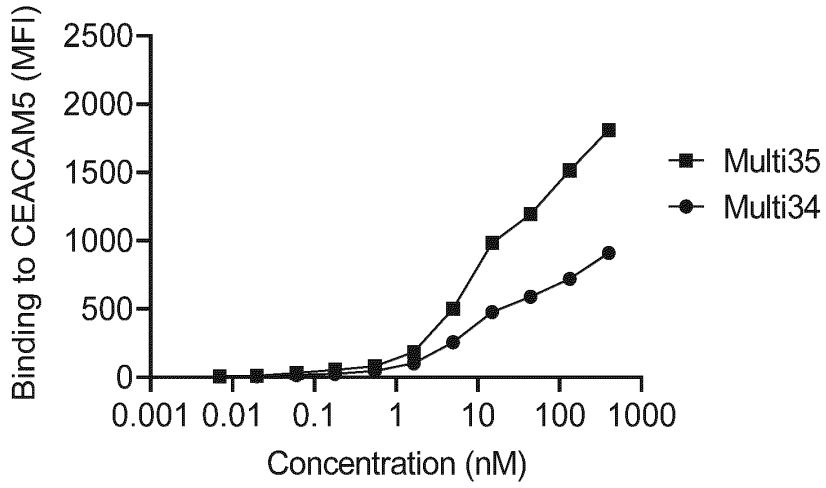

Multi34
Multi46
Multi42
AC_05339
nm
Time (sec)
0
50
100
150
0.1
0.2
0.3
0.5
1
0.02
0.04

Figure 6 (1/3)

A



B

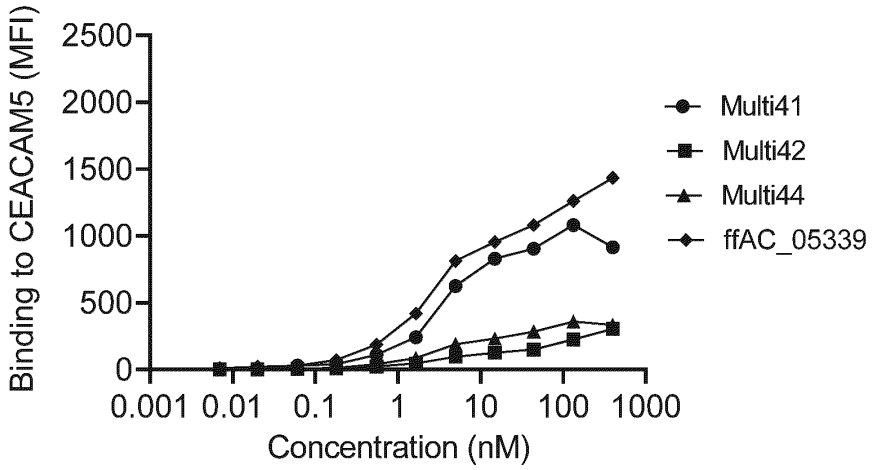
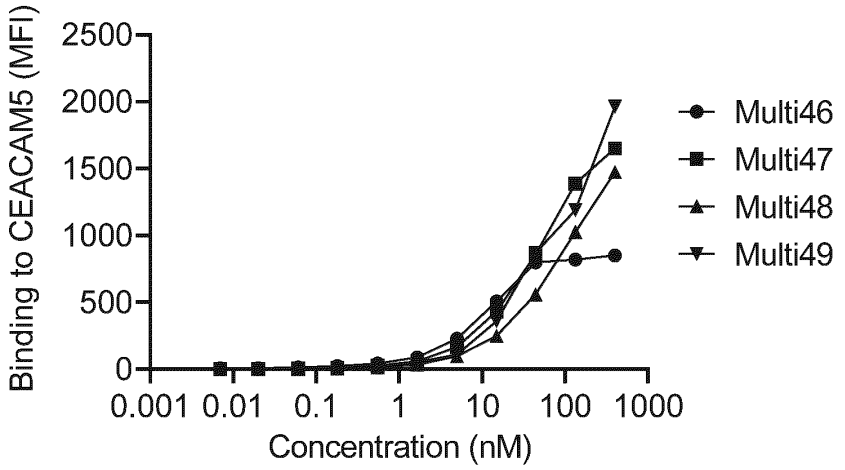


Figure 6 (2/3)

C



D

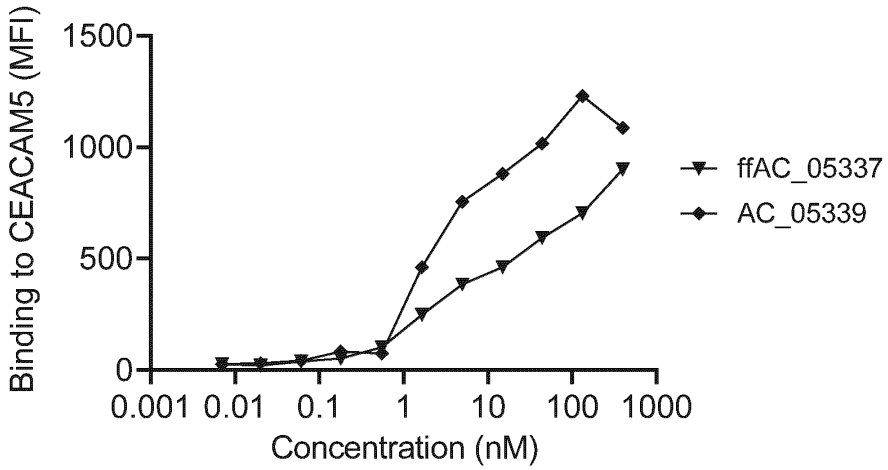


Figure 6 (3/3)

E

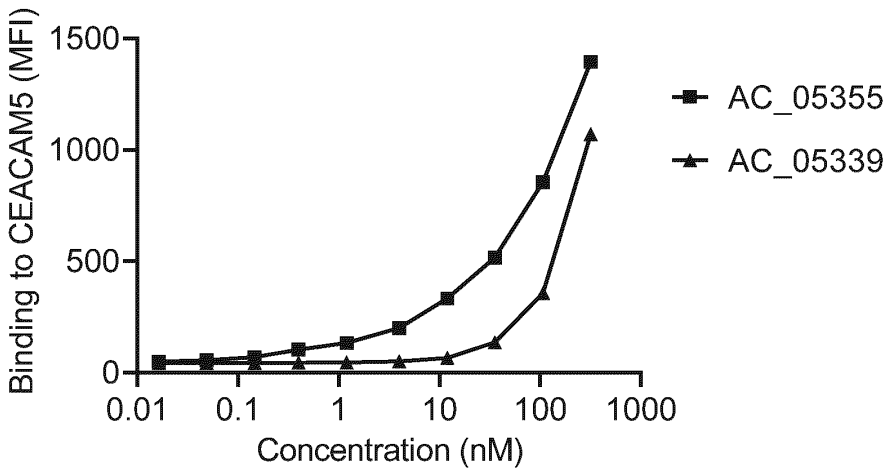
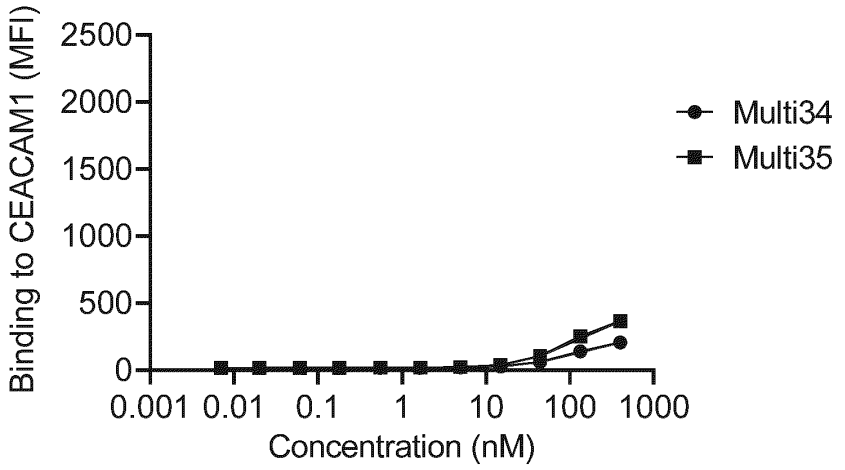

Binding to CEACAM5 (MFI)
1500
1000
500
0
0.01
0.1
1
10
100
1000
Concentration (nM)
AC_05355
AC_05339

Figure 7 (1/2)

A



B

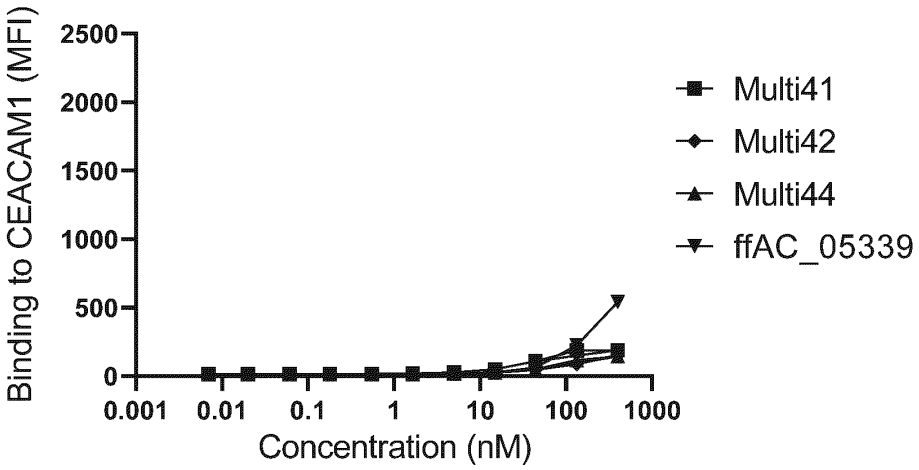
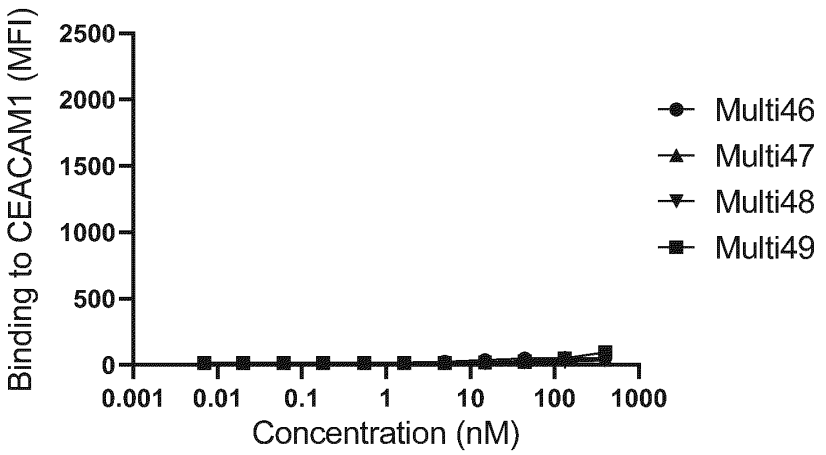


Figure 7 (2/2)

C



D

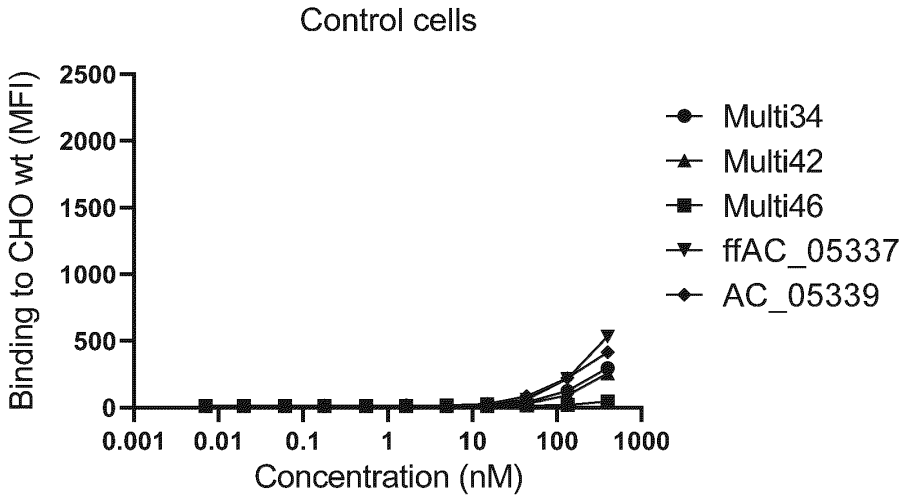
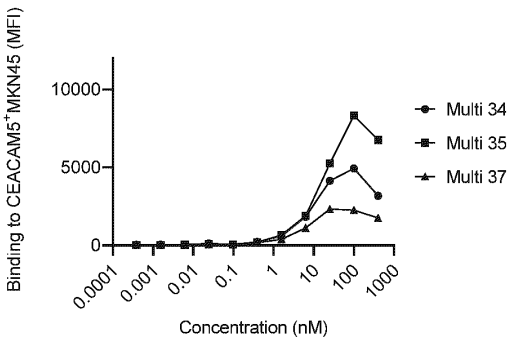
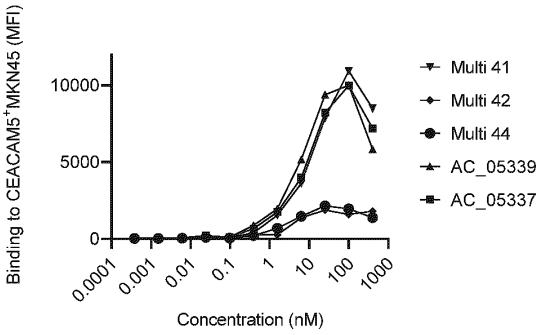


Figure 8 (1/3)

A



B



C

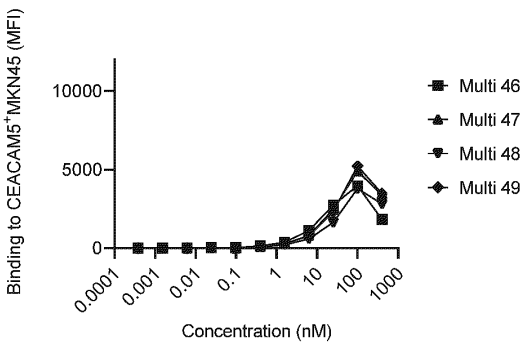


Figure 8 (2/3)

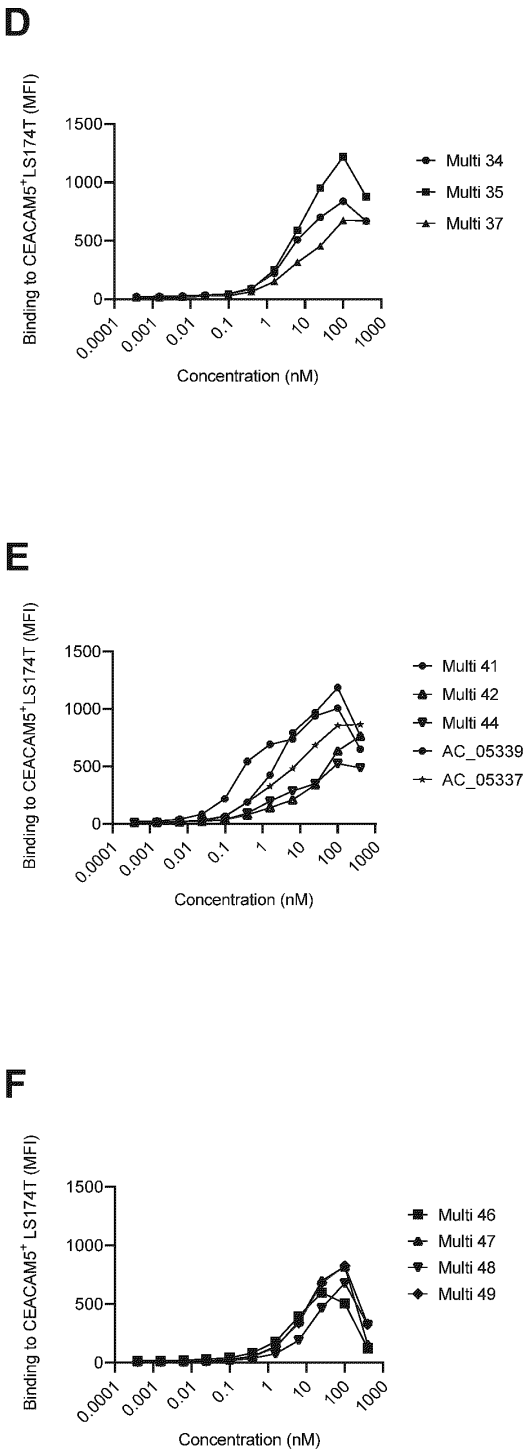

D
Binding to CEACAM5+LS174T (MFI)
1500
1000
500
0
0.0001
0.001
0.01
0.1
1
10
100
1000
Concentration (nM)
Multi 34
Multi 35
Multi 37
E
Binding to CEACAM5+LS174T (MFI)
1500
1000
500
0
0.0001
0.001
0.01
0.1
1
10
100
1000
Concentration (nM)
Multi 41
Multi 42
Multi 44
AC_05339
AC_05337
F
Binding to CEACAM5+ LS174T (MFI)
1500
1000
500
0
0.0001
0.001
0.01
0.1
1
10
100
1000
Concentration (nM)
Multi 46
Multi 47
Multi 48
Multi 49

Figure 8 (3/3)

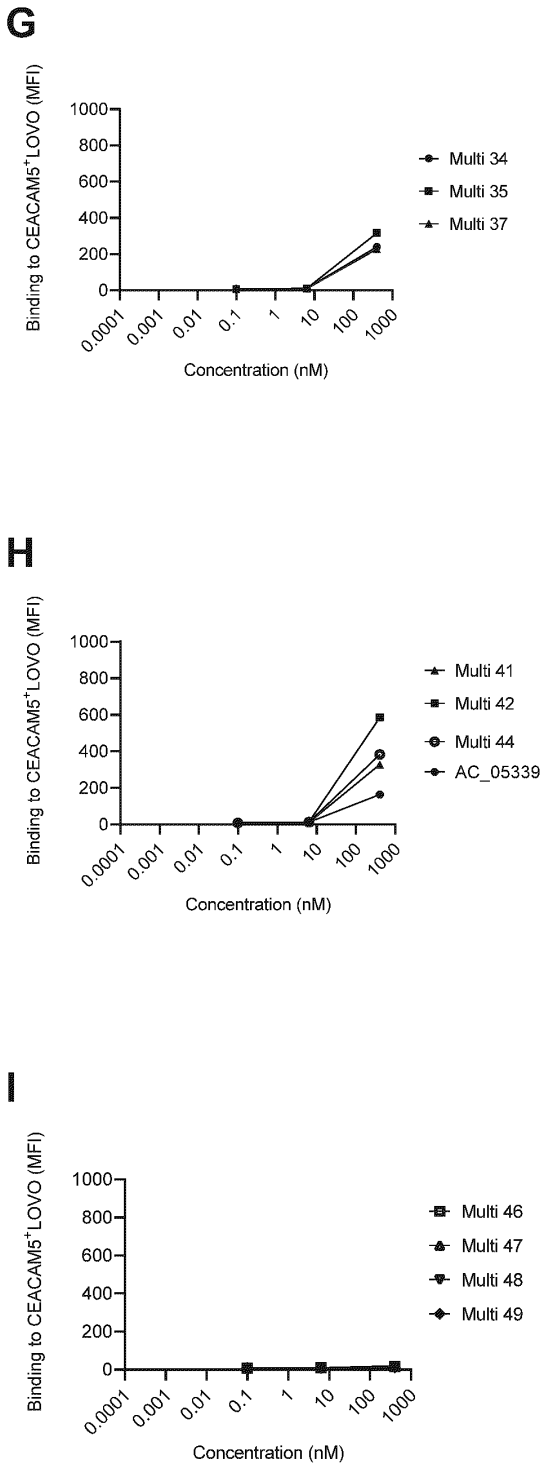

G
Binding to CEACAM5+LOVO (MFI)
1000
800
600
400
200
0
0.0001
0.001
0.01
0.1
1
10
100
1000
Concentration (nM)
Multi 34
Multi 35
Multi 37
H
Binding to CEACAM5+LOVO (MFI)
Concentration (nM)
Multi 41
Multi 42
Multi 44
AC_05339
I
Binding to CEACAM5+LOVO (MFI)
Concentration (nM)
Multi 46
Multi 47
Multi 48
Multi 49

Figure 9 (1/2)

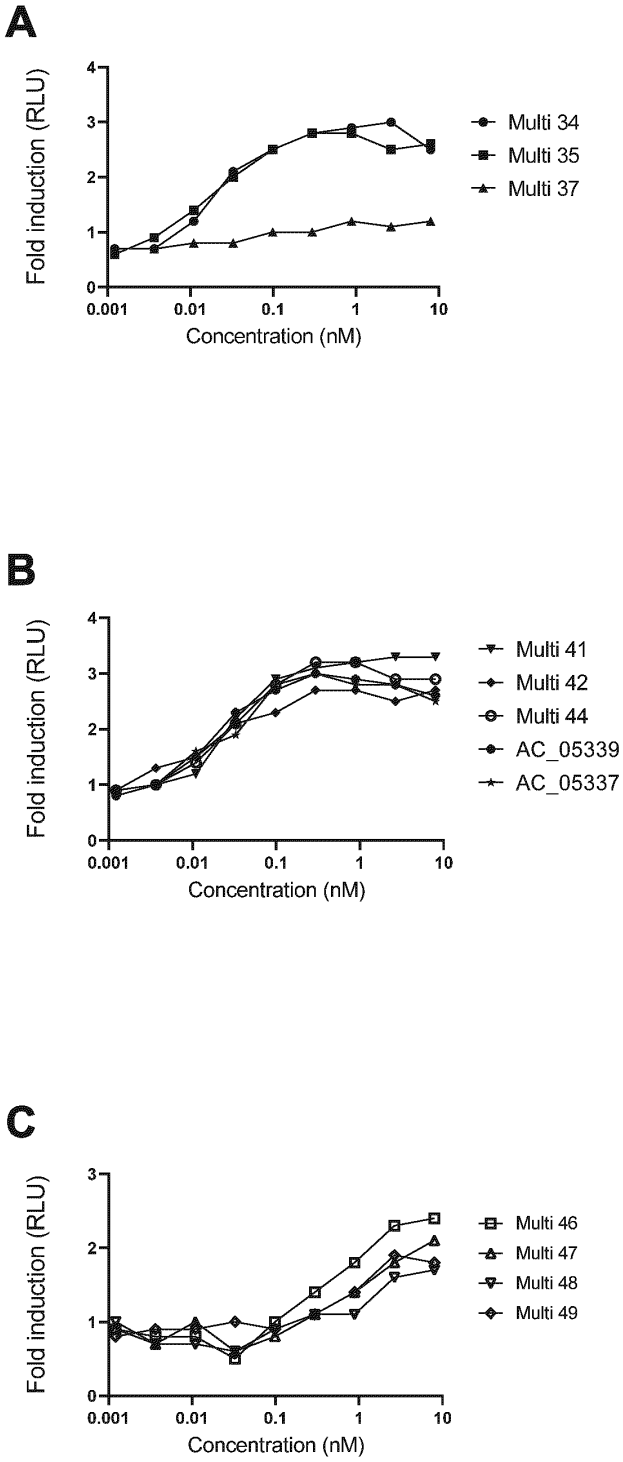
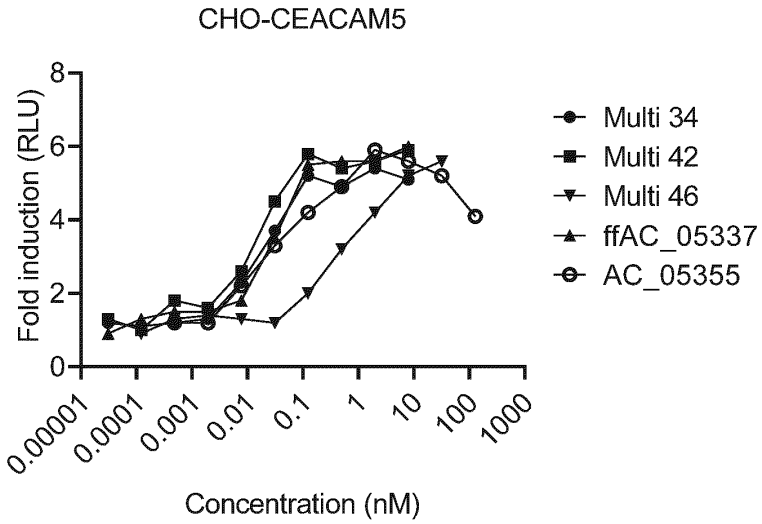

A
Fold induction (RLU)
Concentration (nM)
Multi 34
Multi 35
Multi 37
B
Fold induction (RLU)
Concentration (nM)
Multi 41
Multi 42
Multi 44
AC_05339
AC_05337
C
Fold induction (RLU)
Concentration (nM)
Multi 46
Multi 47
Multi 48
Multi 49

Figure 9 (2/2)

D



E

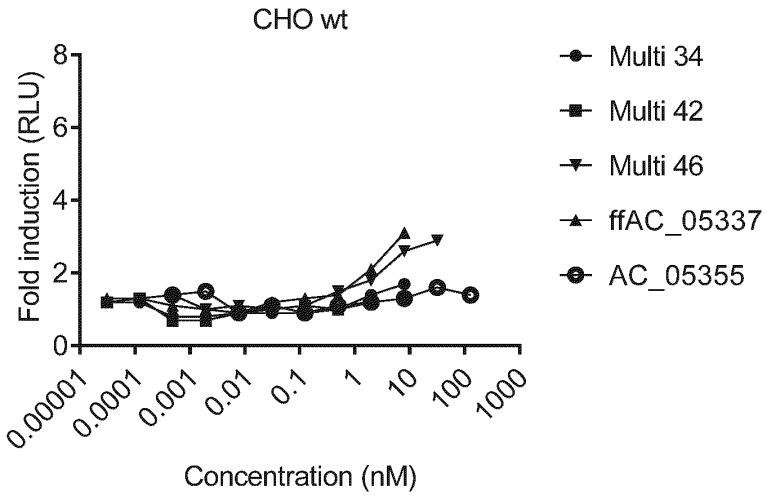


Figure 10 (1/6)

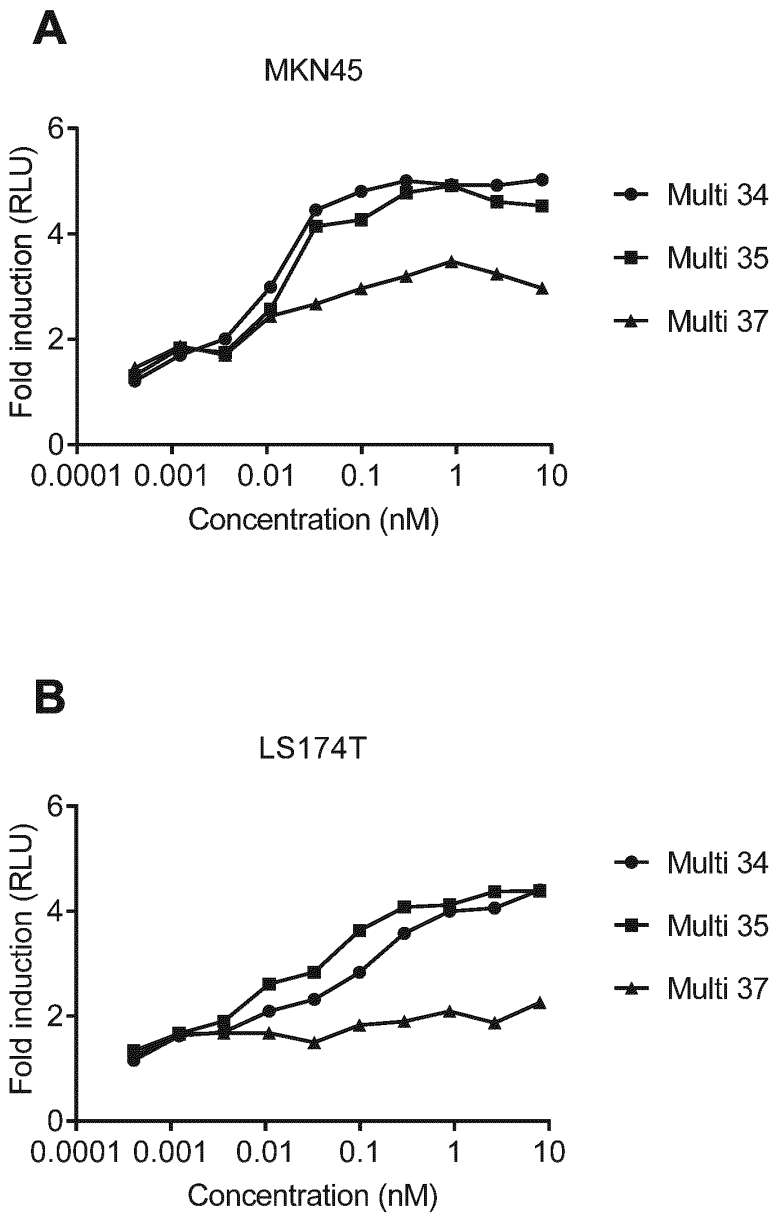

A
MKN45
Fold induction (RLU)
0
2
4
6
0.0001 0.001 0.01 0.1 1 10
Concentration (nM)
Multi 34
Multi 35
Multi 37
B
LS174T
Fold induction (RLU)
0
2
4
6
0.0001 0.001 0.01 0.1 1 10
Concentration (nM)
Multi 34
Multi 35
Multi 37

Figure 10 (2/6)

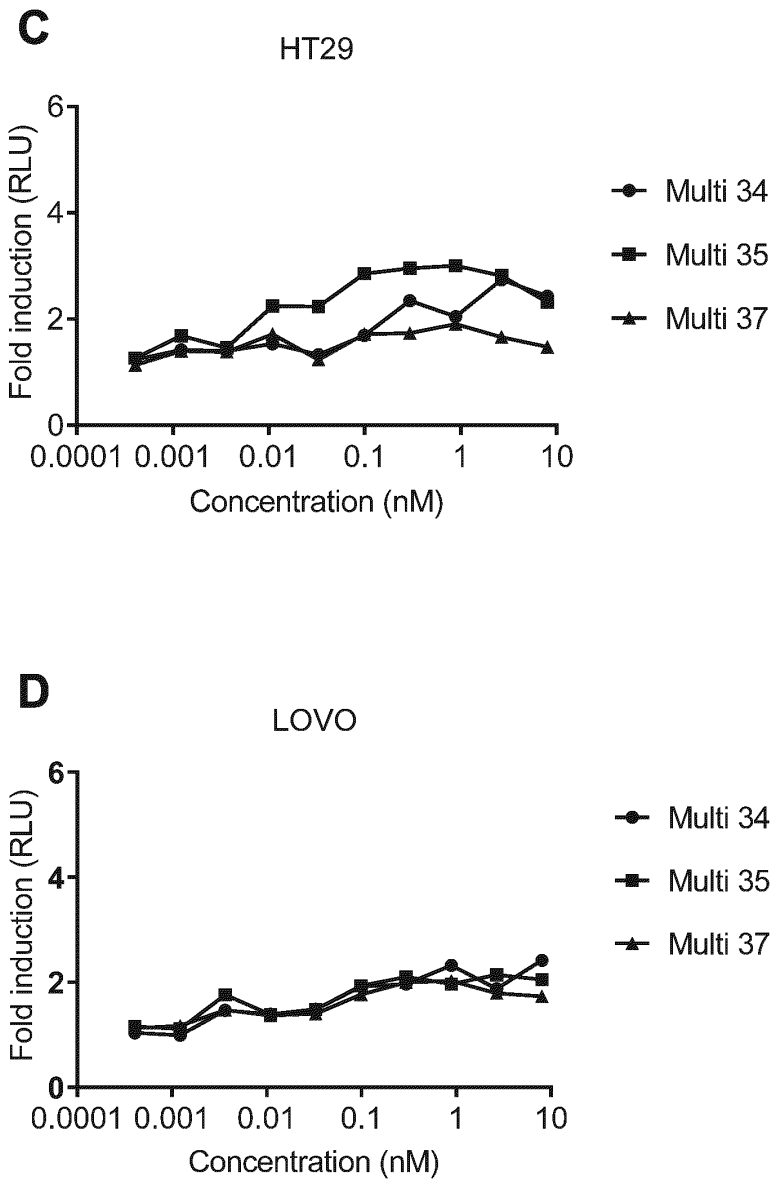

C
HT29
Fold induction (RLU)
0
2
4
6
0.0001 0.001 0.01 0.1 1 10
Concentration (nM)
Multi 34
Multi 35
Multi 37
D
LOVO
Fold induction (RLU)
0
2
4
6
0.0001 0.001 0.01 0.1 1 10
Concentration (nM)
Multi 34
Multi 35
Multi 37

Figure 10 (3/6)

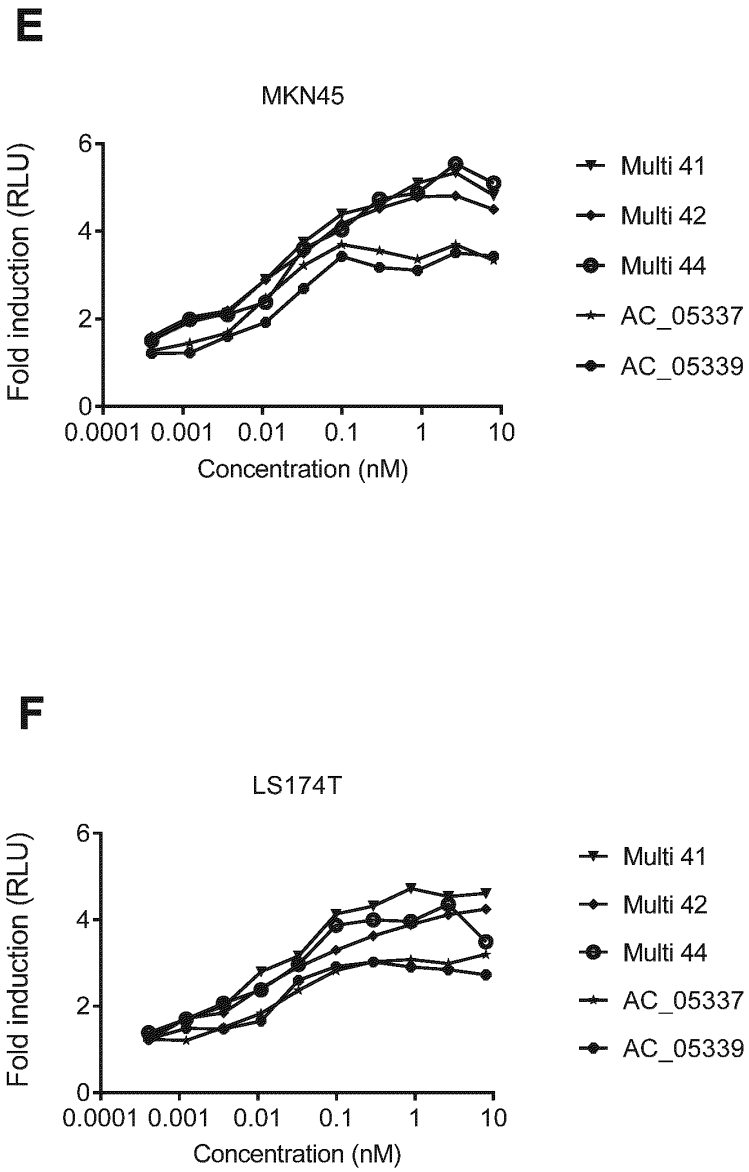
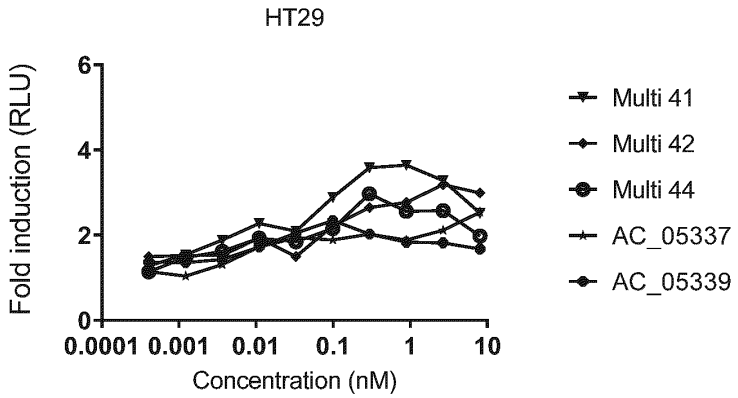

E
MKN45
Fold induction (RLU)
0
2
4
6
0.0001 0.001 0.01 0.1 1 10
Concentration (nM)
Multi 41
Multi 42
Multi 44
AC_05337
AC_05339
F
LS174T
Fold induction (RLU)
0
2
4
6
0.0001 0.001 0.01 0.1 1 10
Concentration (nM)
Multi 41
Multi 42
Multi 44
AC_05337
AC_05339

Figure 10 (4/6)

G



H

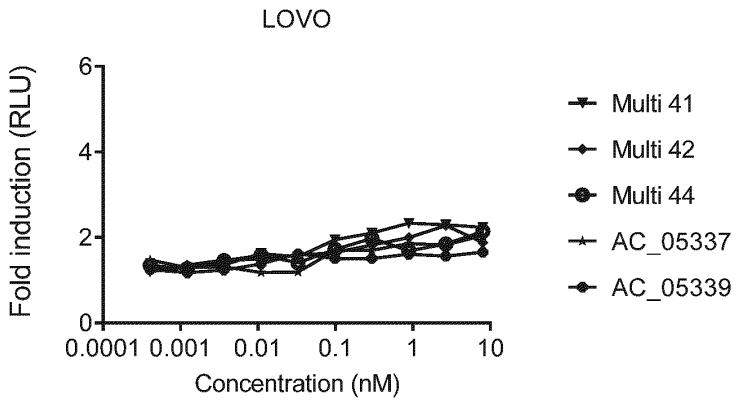
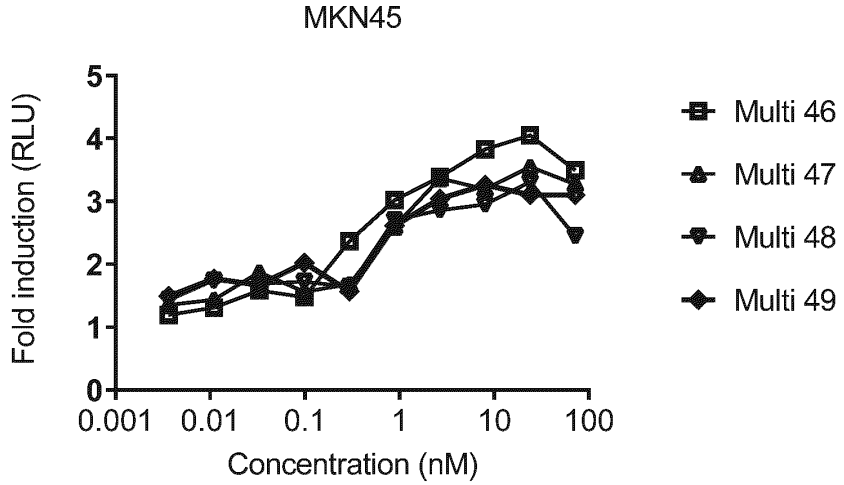


Figure 10 (5/6)

I



J

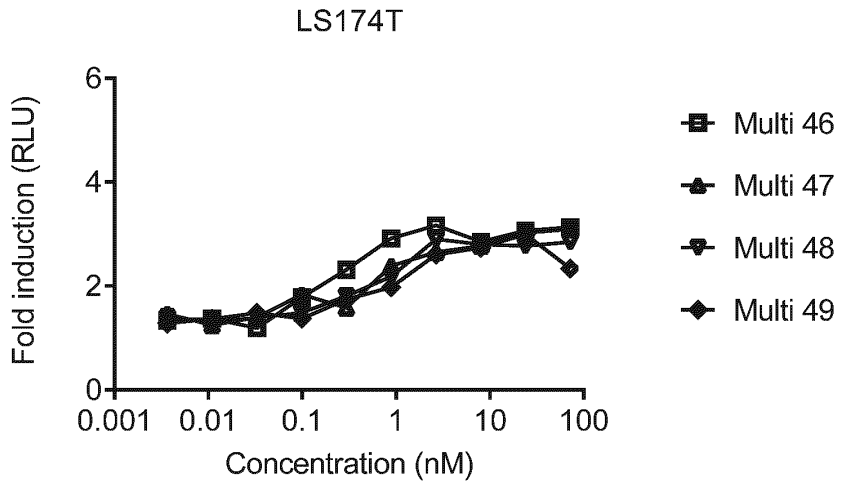
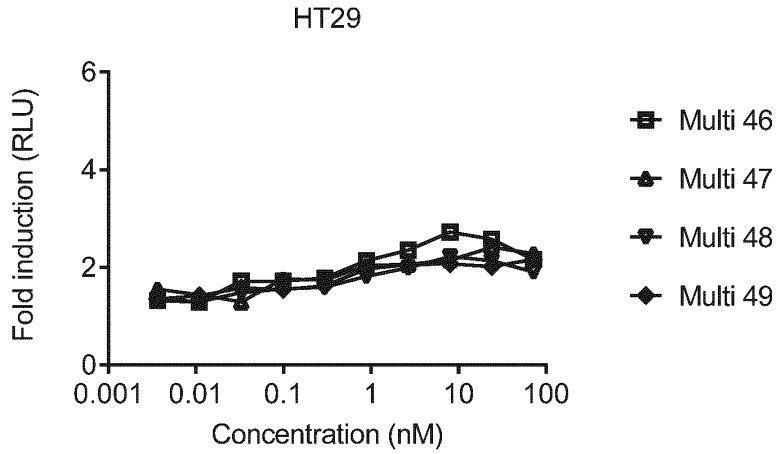


Figure 10 (6/6)

K



L

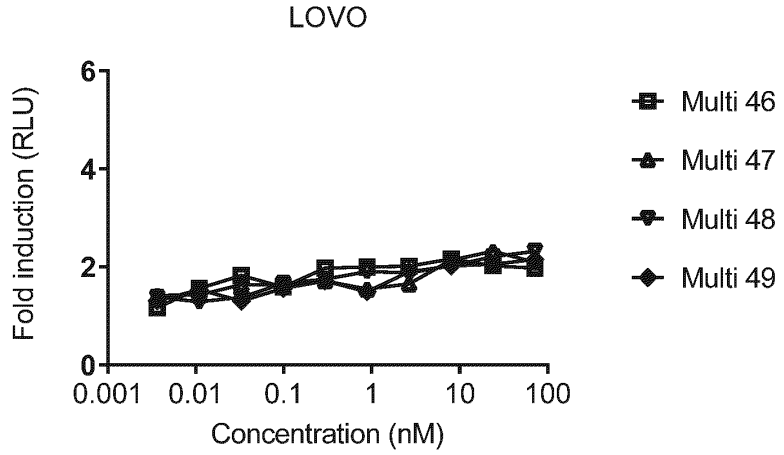


Figure 11 (1/5)

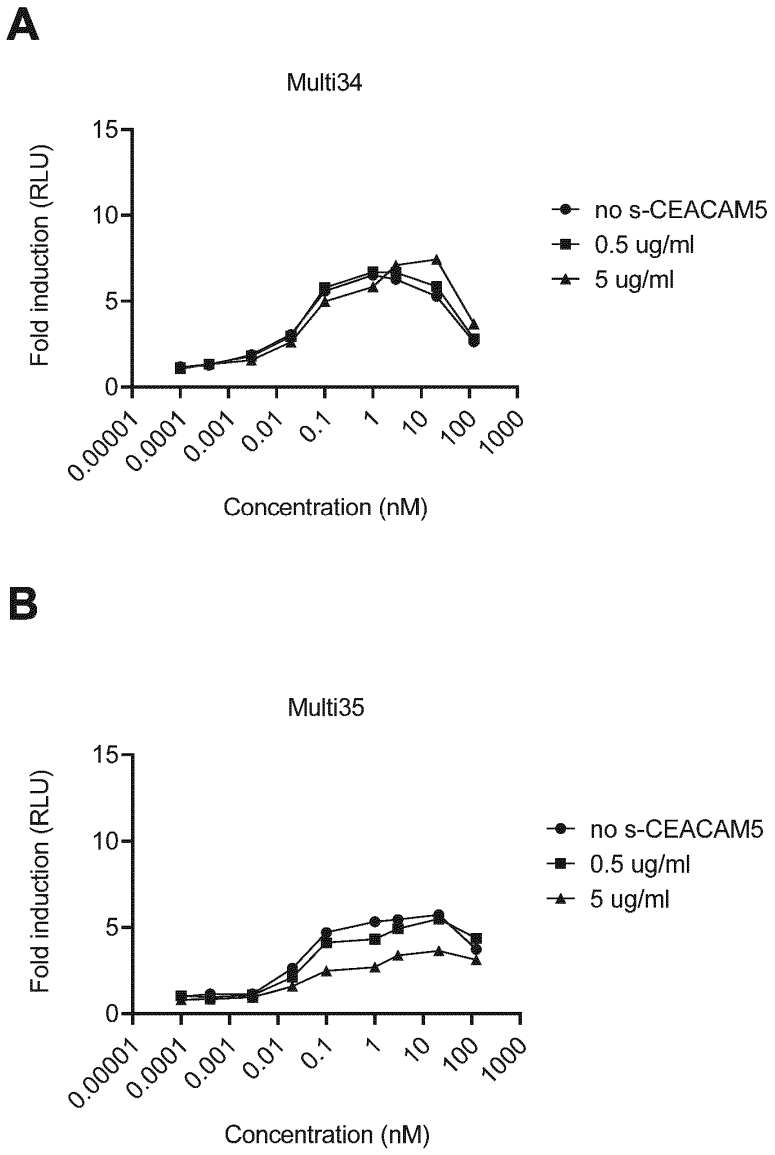
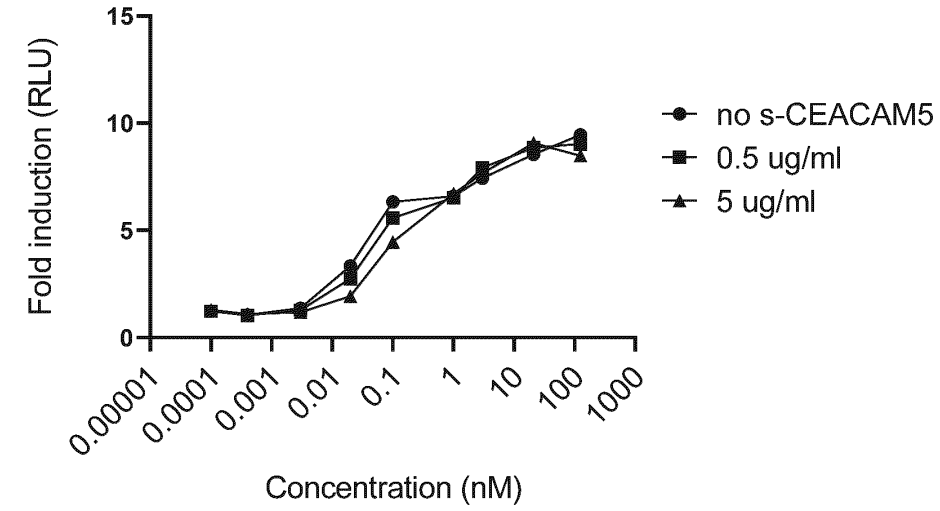

A
Multi34
Fold induction (RLU)
15
10
5
0
0.00001
0.0001
0.001
0.01
0.1
1
10
100
1000
Concentration (nM)
no s-CEACAM5
0.5 ug/ml
5 ug/ml
B
Multi35
Fold induction (RLU)
15
10
5
0
0.00001
0.0001
0.001
0.01
0.1
1
10
100
1000
Concentration (nM)
no s-CEACAM5
0.5 ug/ml
5 ug/ml

Figure 11 (2/5)

C



D

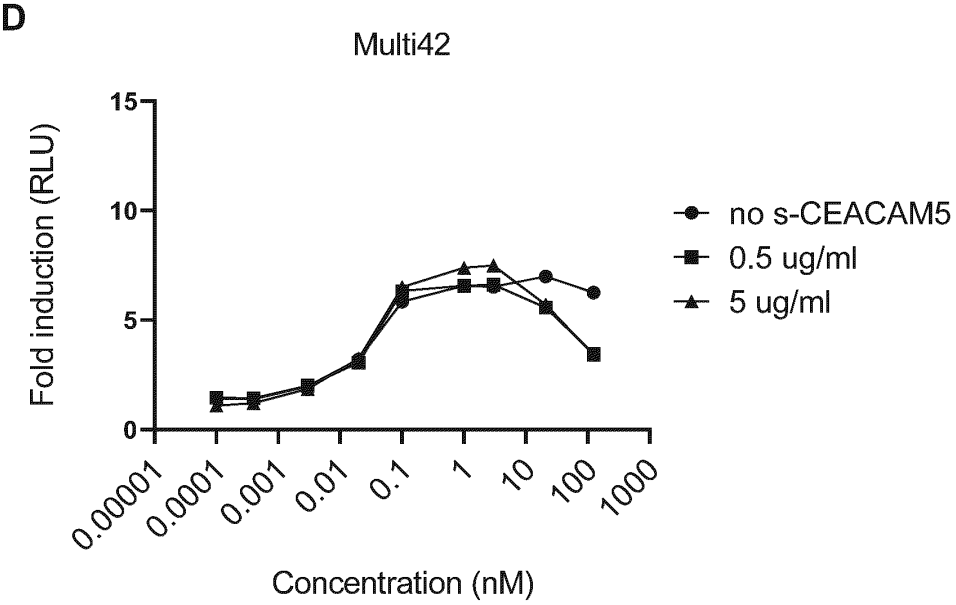


Figure 11 (3/5)

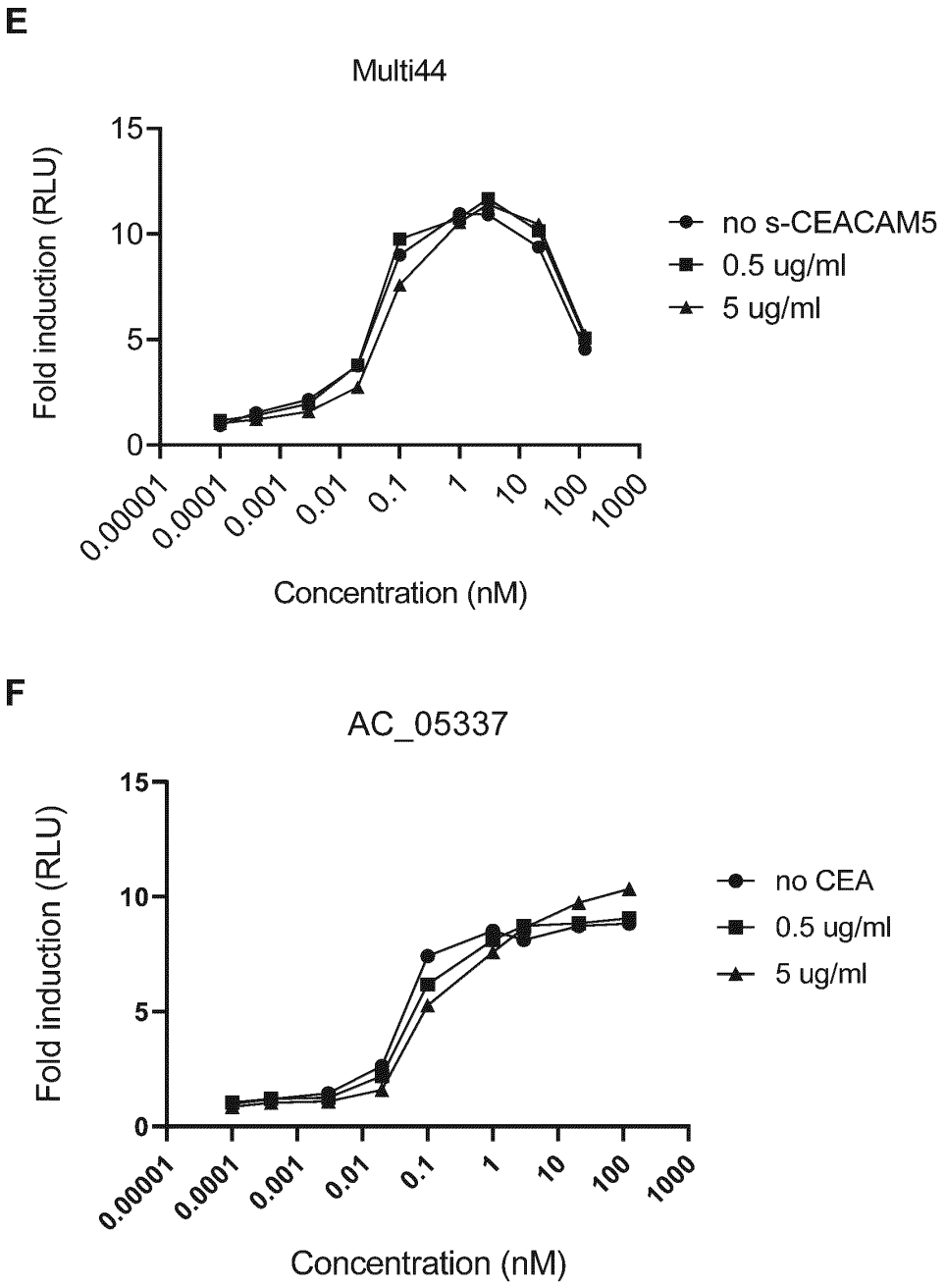
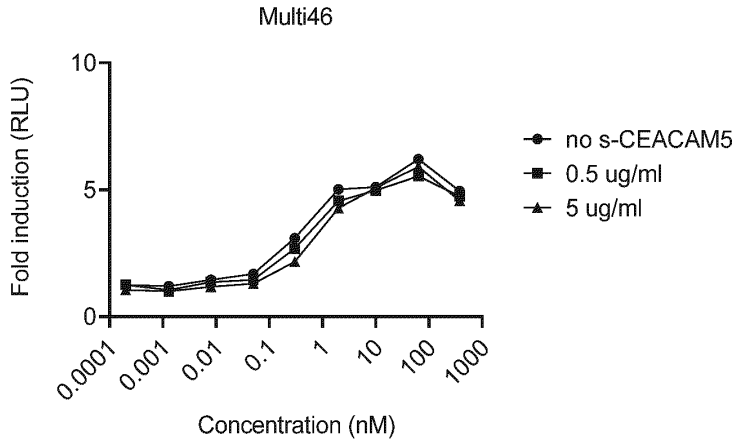

E
Multi44
Fold induction (RLU)
15
10
5
0
0.00001
0.0001
0.001
0.01
0.1
1
10
100
1000
Concentration (nM)
no s-CEACAM5
0.5 ug/ml
5 ug/ml
F
AC_05337
Fold induction (RLU)
15
10
5
0
0.00001
0.0001
0.001
0.01
0.1
1
10
100
1000
Concentration (nM)
no CEA
0.5 ug/ml
5 ug/ml

Figure 11 (4/5)

G



H

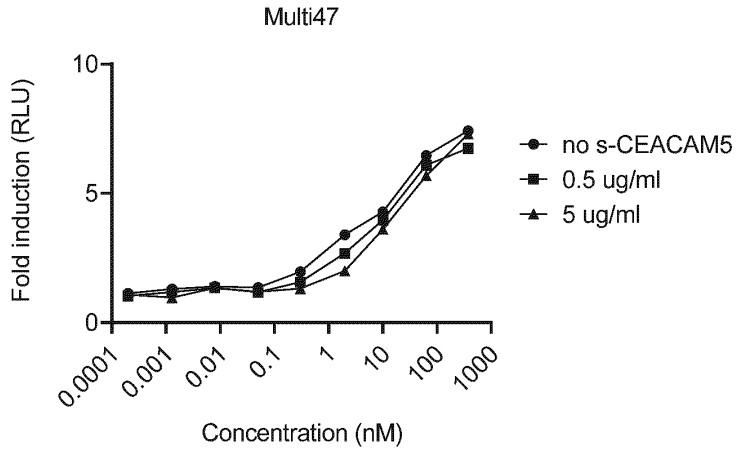
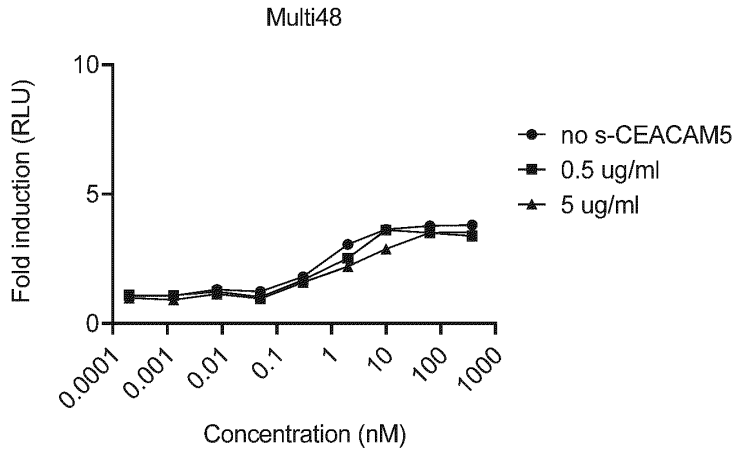


Figure 11 (5/5)

I



J

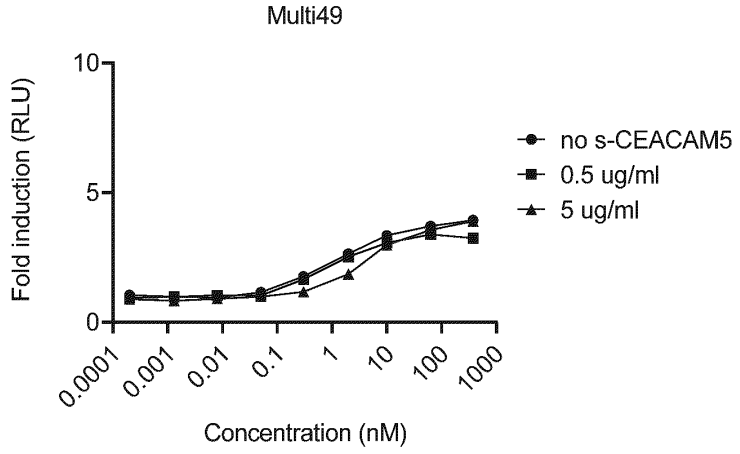


Figure 12

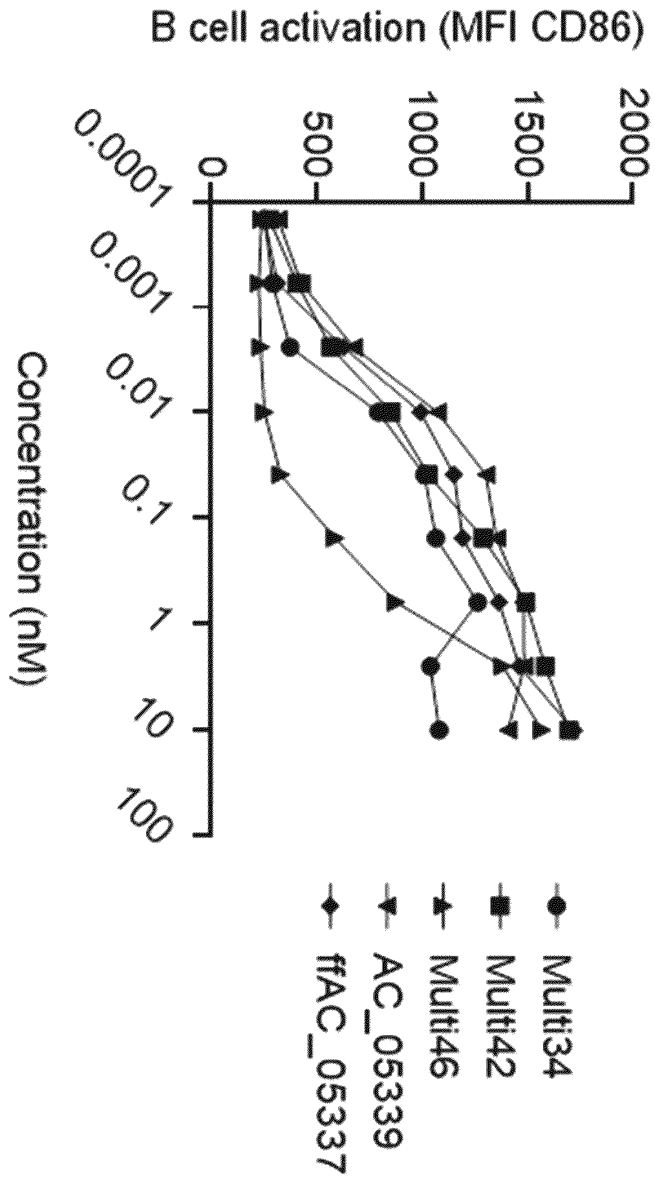

B cell activation (MFI CD86)
0
500
1000
1500
2000
Concentration (nM)
0.0001
0.001
0.01
0.1
1
10
100
Multi34
Multi42
Multi46
AC_05339
ffAC_05337

Figure 13

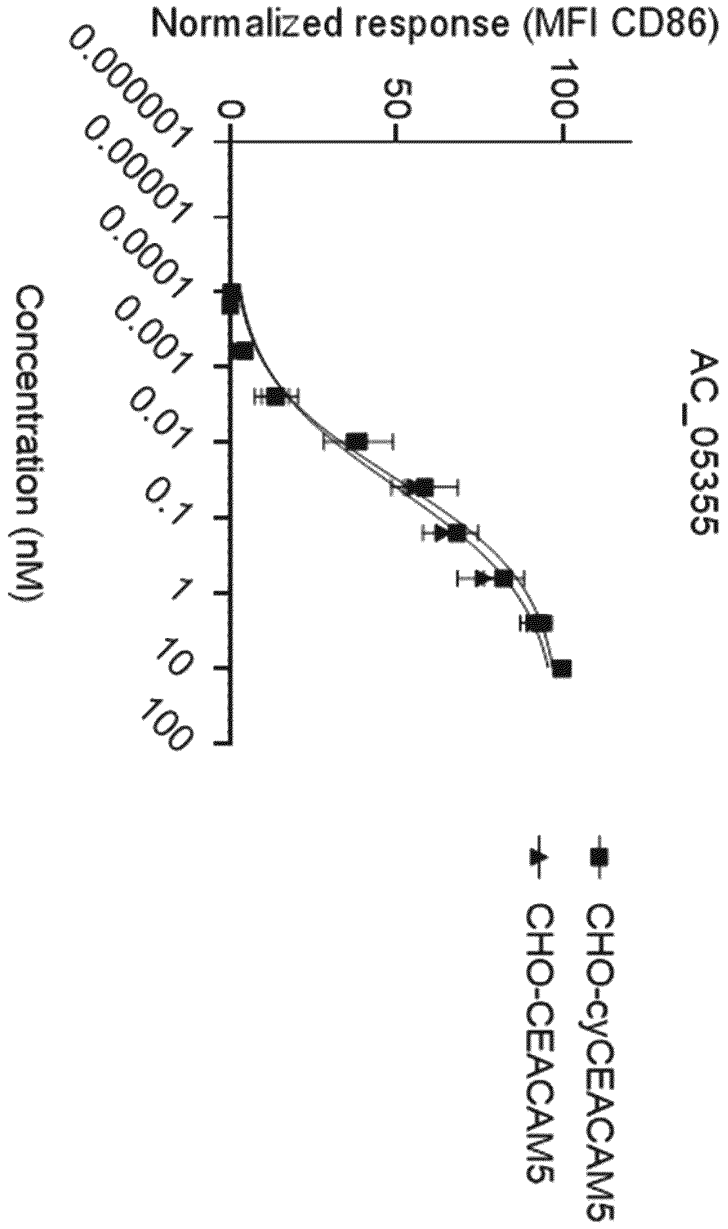

Normalized response (MFI CD86)
0
50
100
Concentration (nM)
0.000001
0.00001
0.0001
0.001
0.01
0.1
1
10
100
AC_05355
CHO-cyCEACAM5
CHO-CEACAM5

Figure 14

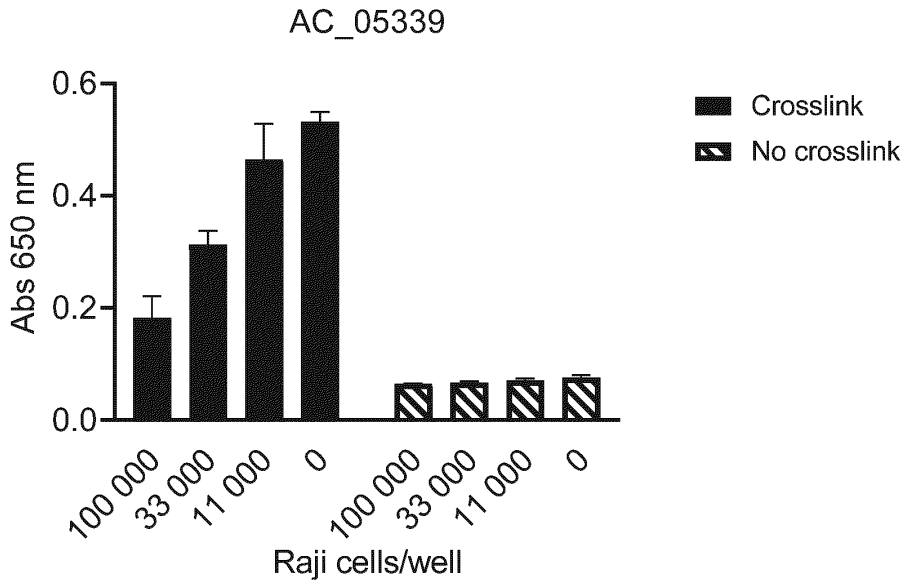

AC_05339
Abs 650 nm
0.6
0.4
0.2
0.0
100 000
33 000
11 000
0
100 000
33 000
11 000
0
Raji cells/well
Crosslink
No crosslink

Figure 15

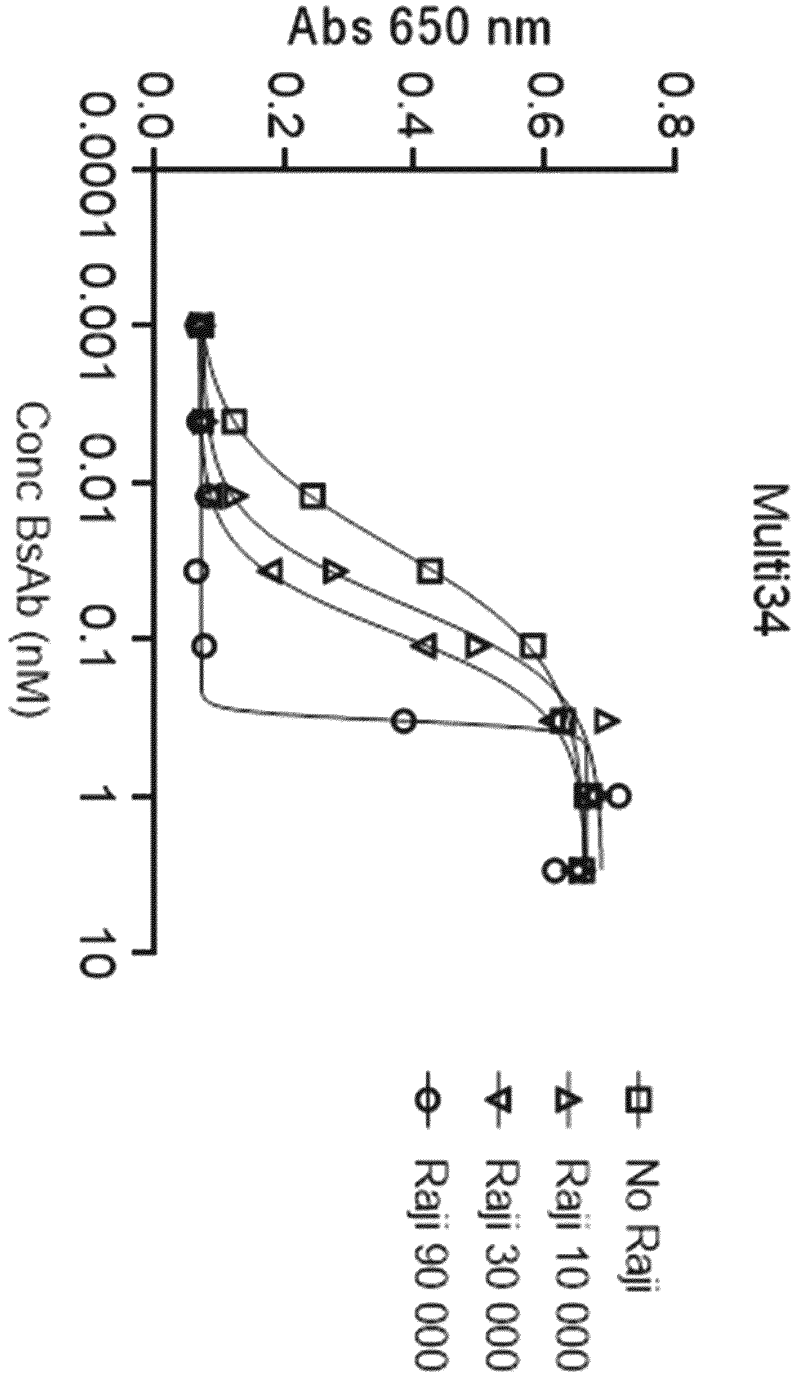

Abs 650 nm
0.0
0.2
0.4
0.6
0.8
0.0001
0.001
0.01
0.1
1
10
Conc BsAb (nM)
Multi34
No Raji
Raji 10 000
Raji 30 000
Raji 90 000

Figure 16

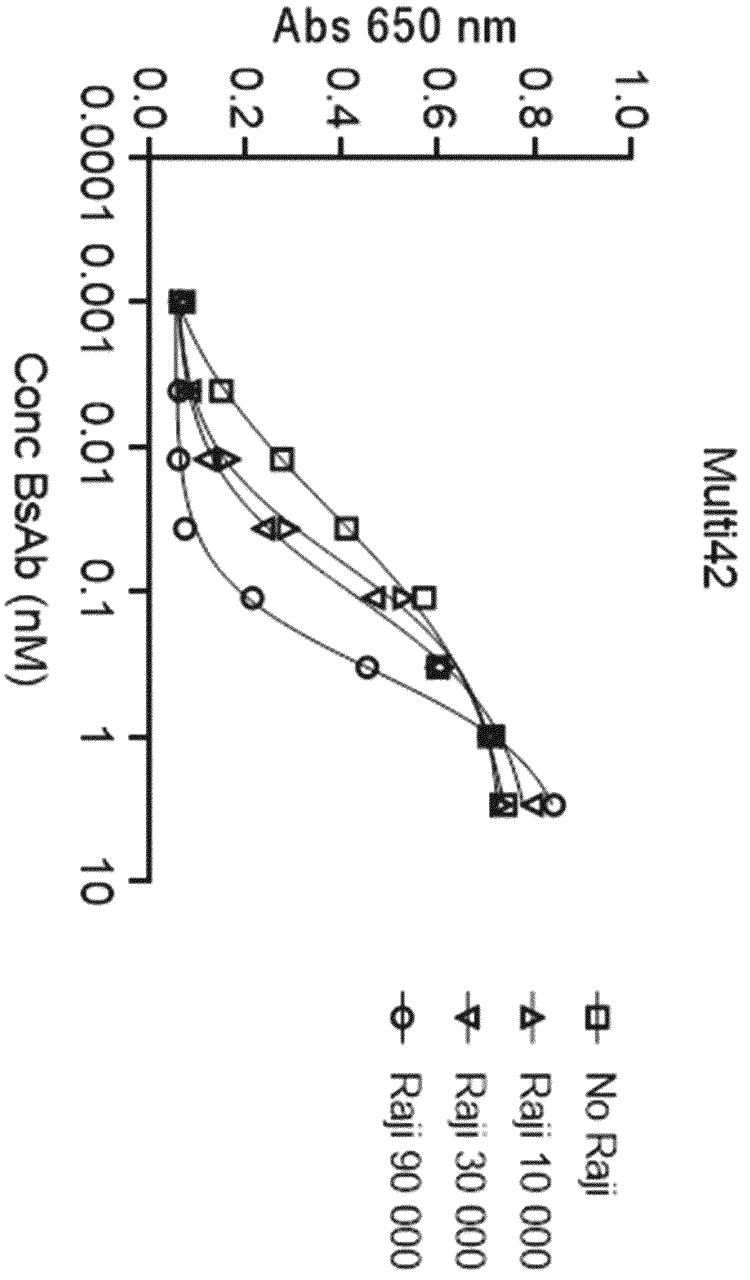

Abs 650 nm
0.0
0.2
0.4
0.6
0.8
1.0
0.0001
0.001
0.01
0.1
1
10
Conc BsAb (nM)
Multi42
No Raji
Raji 10 000
Raji 30 000
Raji 90 000

Figure 17

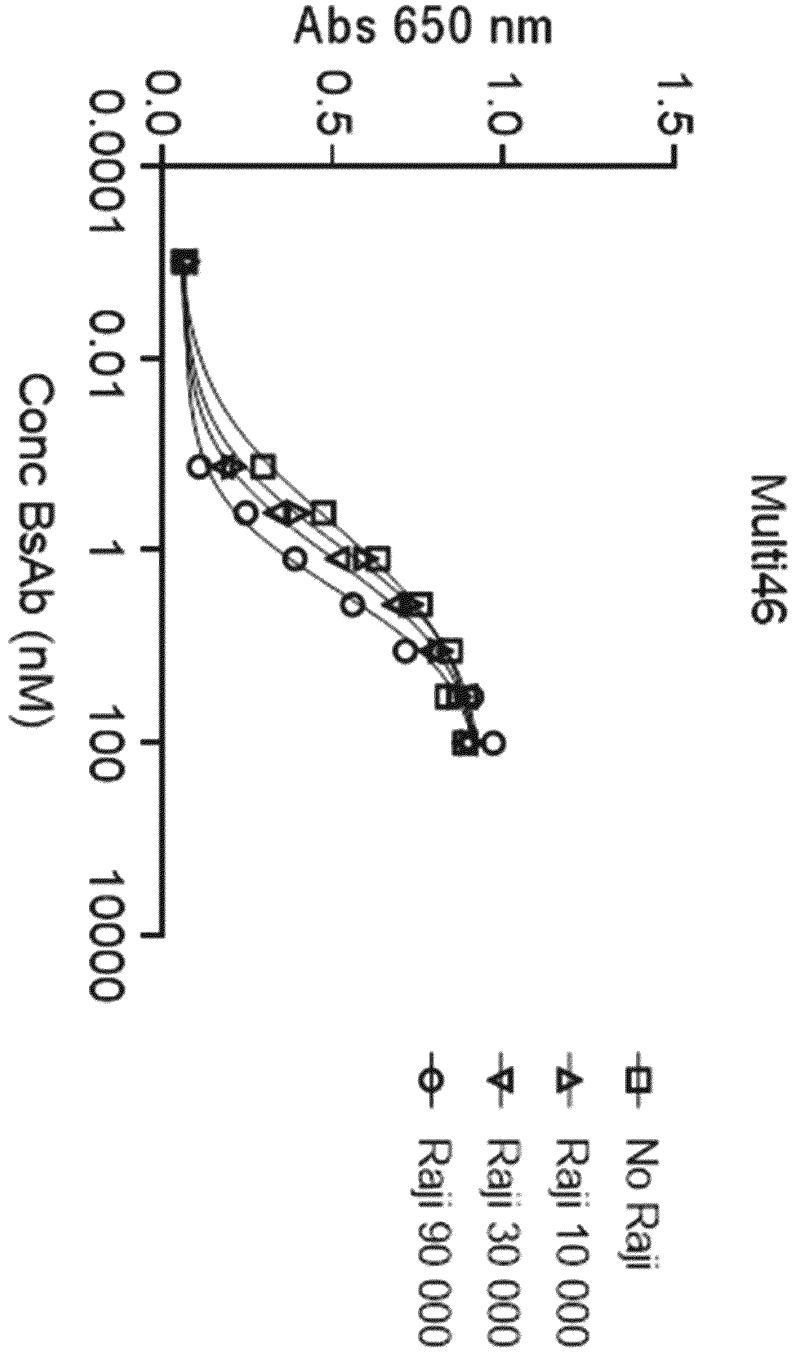

Abs 650 nm
0.0
0.5
1.0
1.5
0.0001
0.01
1
100
10000
Conc BsAb (nM)
Multi46
No Raji
Raji 10 000
Raji 30 000
Raji 90 000

Figure 18

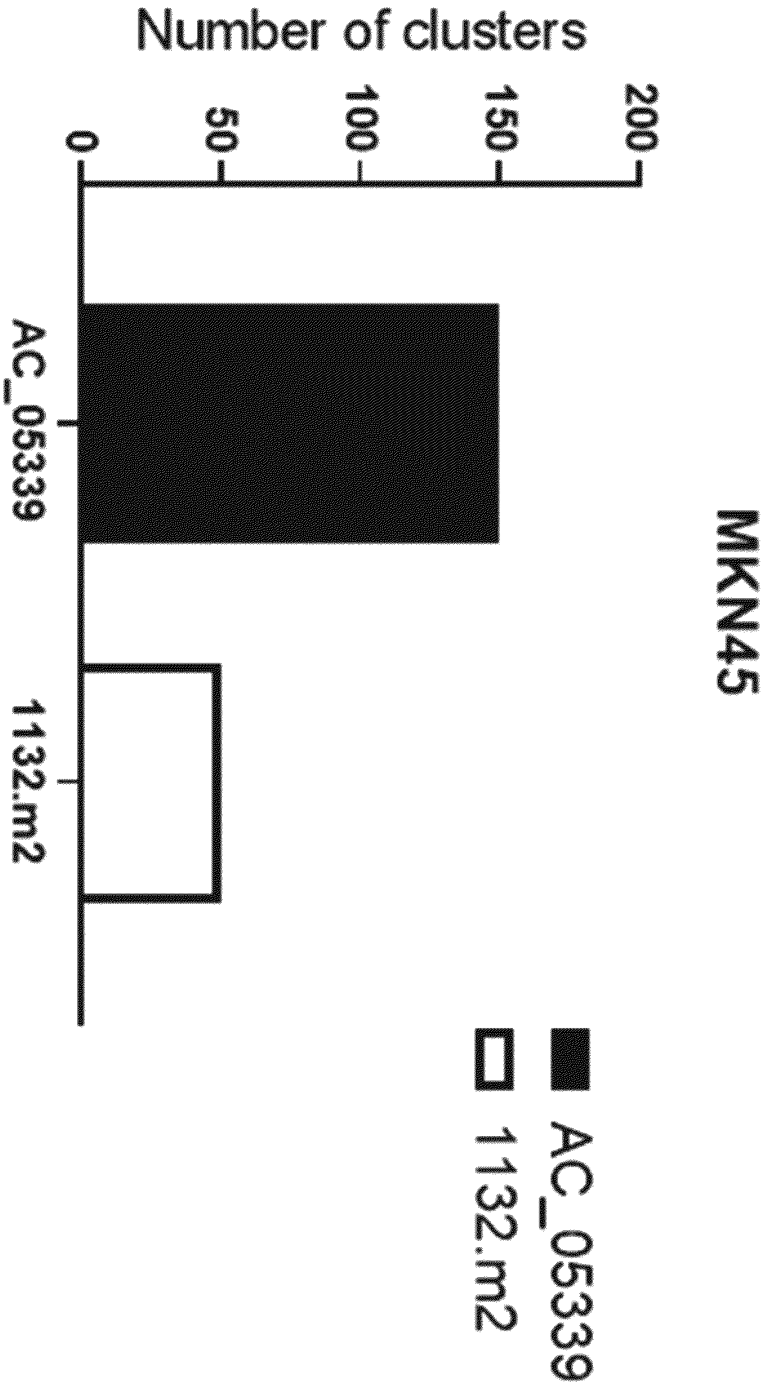

Number of clusters
0
50
100
150
200
AC_05339
1132.m2
MKN45
AC_05339
1132.m2

Figure 19 (1/2)

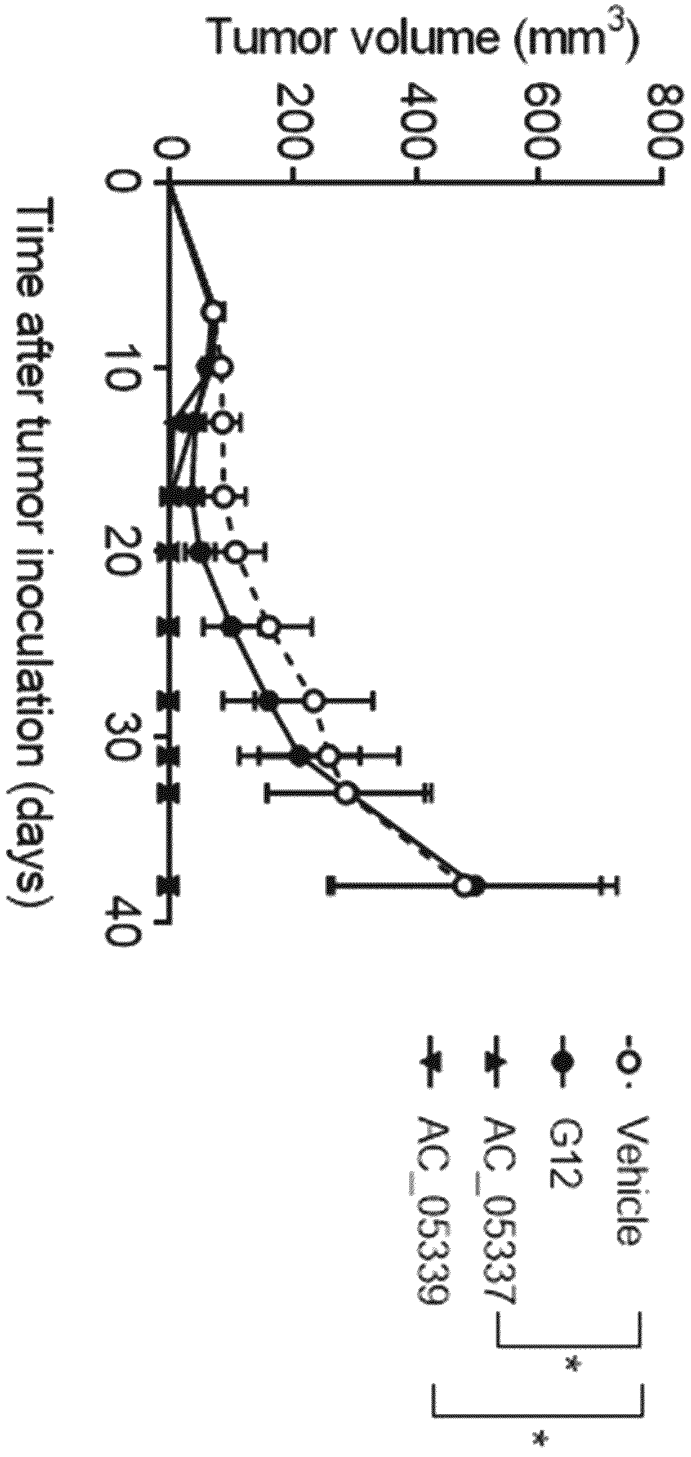

Tumor volume (mm3)
0
200
400
600
800
0
10
20
30
40
Time after tumor inoculation (days)
Vehicle
G12
AC_05337
AC_05339
*
*

Figure 19 (2/2)

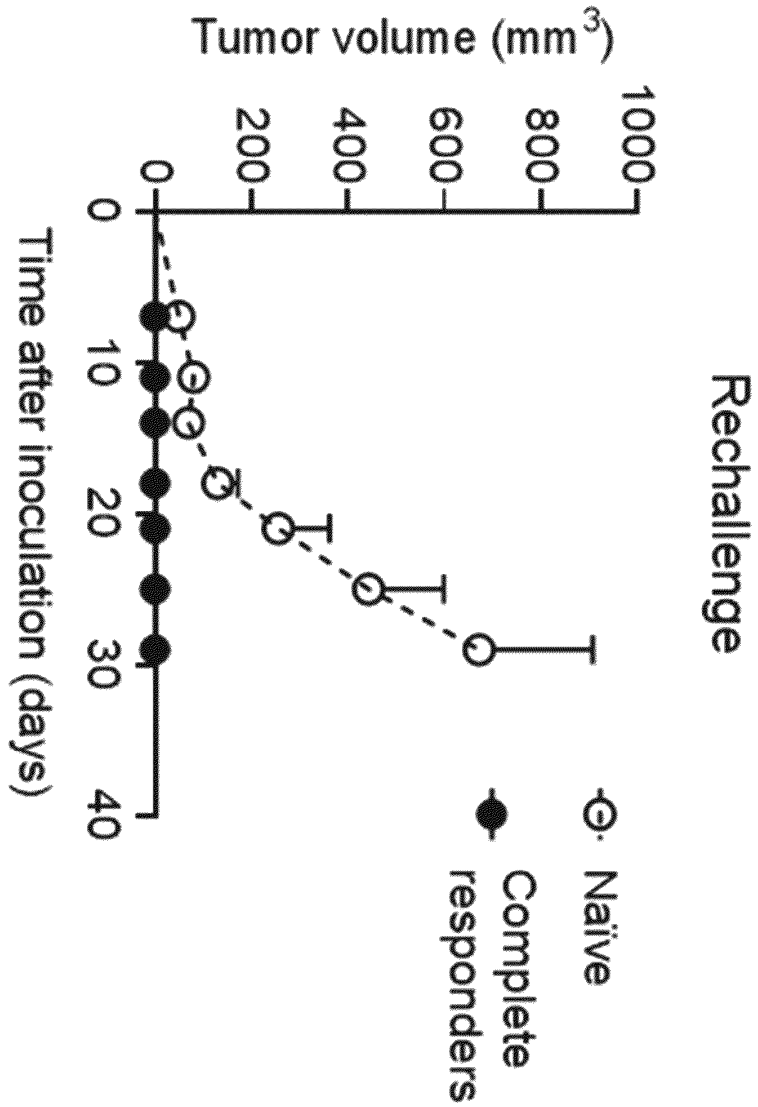

Tumor volume (mm3)
0
200
400
600
800
1000
0
10
20
30
40
Time after inoculation (days)
Rechallenge
Naïve
Complete responders

Figure 20

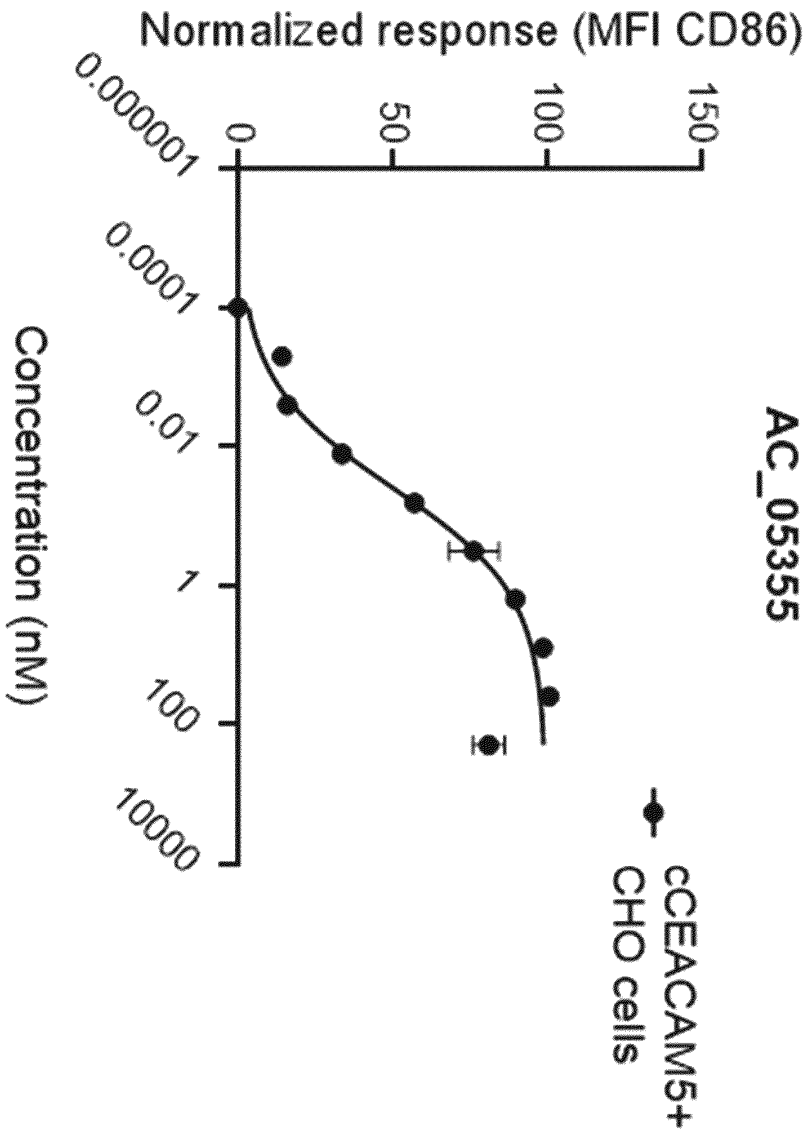

Normalized response (MFI CD86)
0
50
100
150
Concentration (nM)
0.000001
0.0001
0.01
1
100
10000
AC_05355
cCEACAM5+
CHO cells

Figure 21

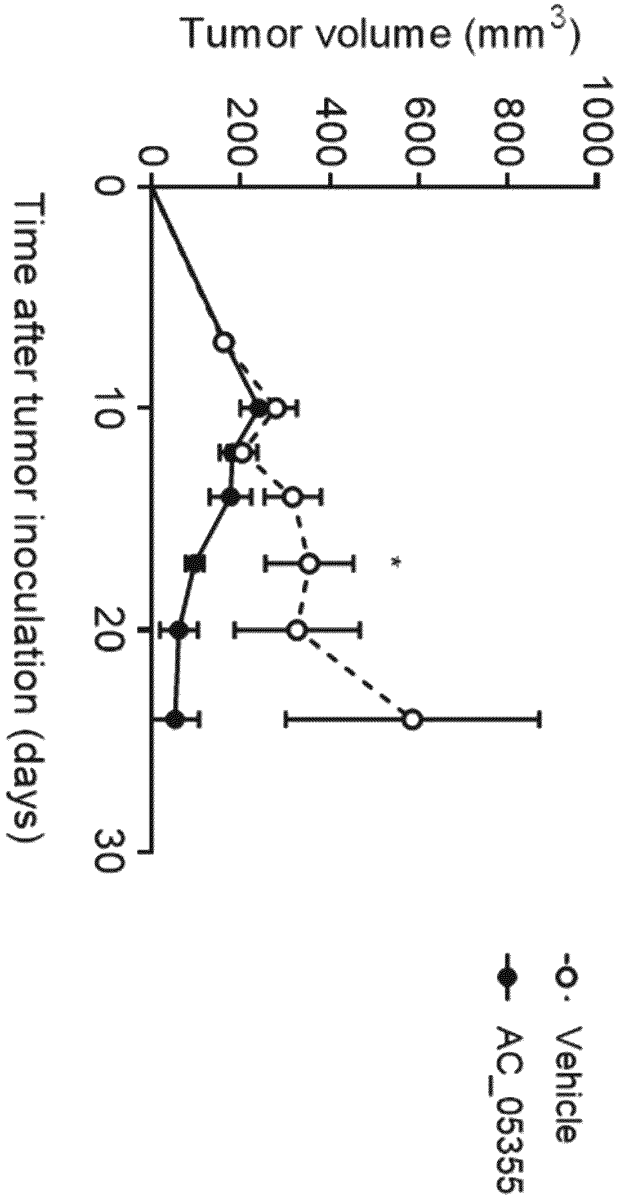

Tumor volume (mm3)
0
200
400
600
800
1000
0
10
20
30
Time after tumor inoculation (days)
*
Vehicle
AC_05355

Figure 22

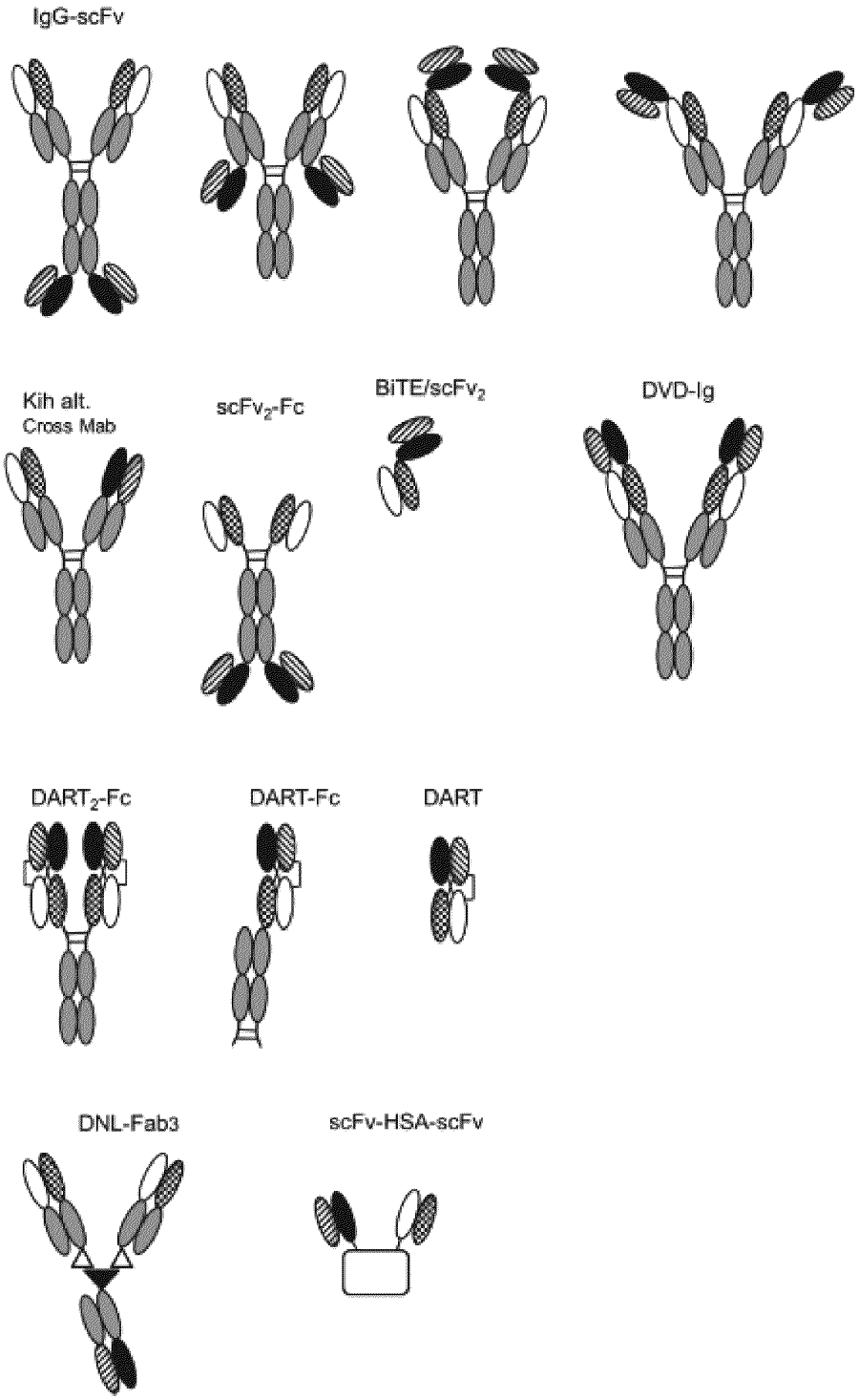

IgG-scFv
Kih alt.
Cross Mab
scFv2-Fc
BiTE/scFv2
DVD-Ig
DART2-Fc
DART-Fc
DART
DNL-Fab3
scFv-HSA-scFv

Figure 23

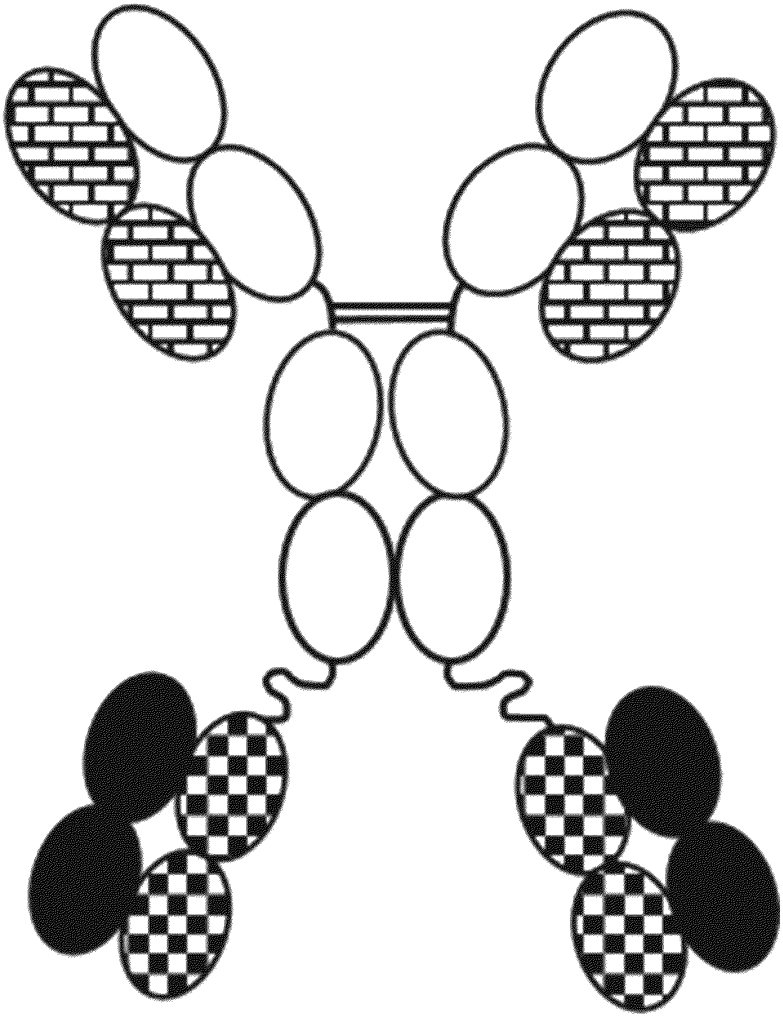


Figure 24

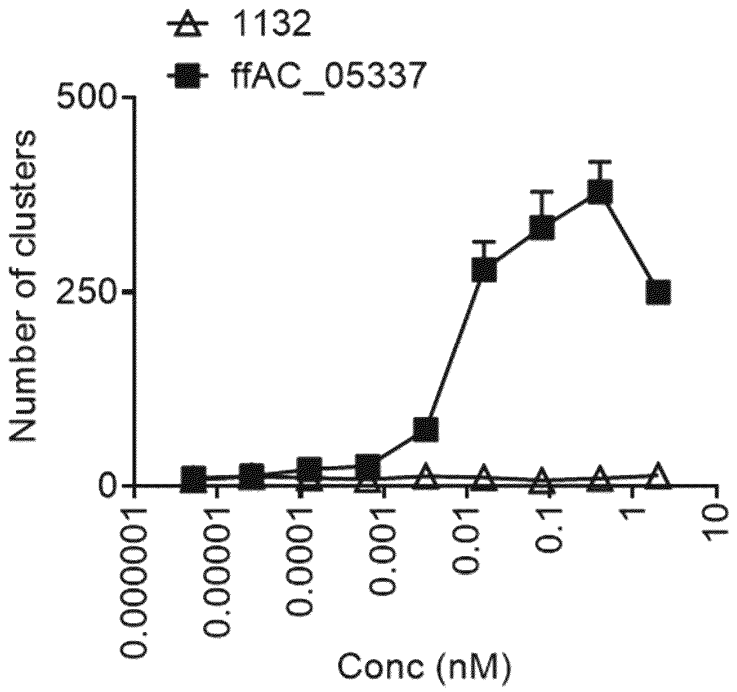

1132
ffAC_05337
500
250
0
Number of clusters
0.000001
0.00001
0.0001
0.001
0.01
0.1
1
10
Conc (nM)

Figure 25 (1/2)

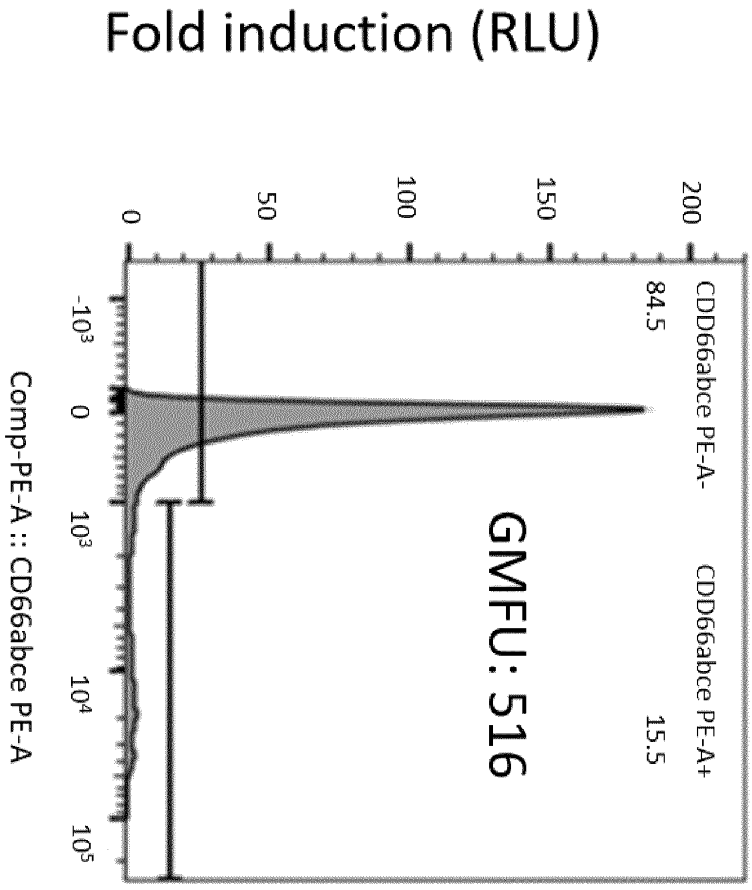

Fold induction (RLU)
0
50
100
150
200
CDD66abce PE-A-
84.5
CDD66abce PE-A+
15.5
GMFU: 516
-10³
0
10³
10⁴
10⁵
Comp-PE-A :: CD66abce PE-A

Figure 25 (2/2)

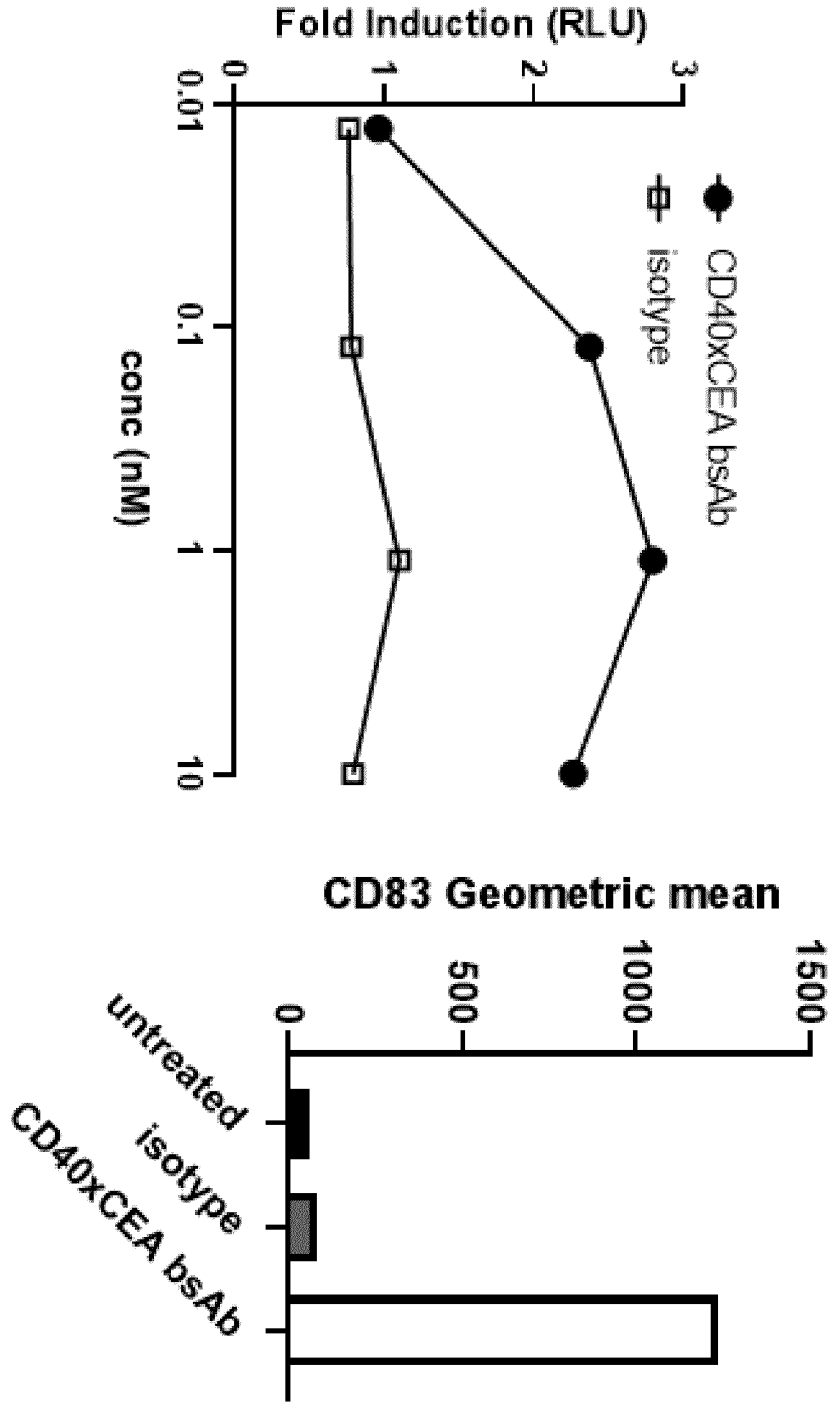

Fold Induction (RLU)
0
1
2
3
conc (nM)
0.01
0.1
1
10
isotype
CD40xCEA bsAb
CD83 Geometric mean
0
500
1000
1500
untreated
isotype
CD40xCEA bsAb

Figure 26

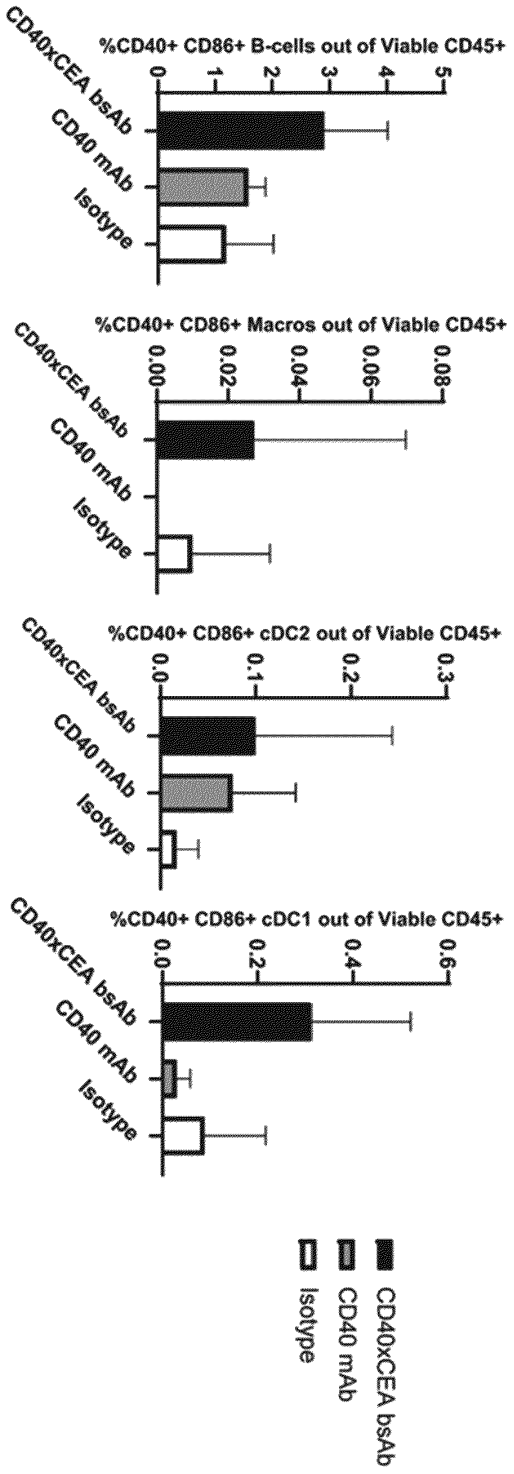

%CD40+ CD86+ B-cells out of Viable CD45+
0
1
2
3
4
5
CD40xCEA bsAb
CD40 mAb
Isotype
%CD40+ CD86+ Macros out of Viable CD45+
0.00
0.02
0.04
0.06
0.08
CD40xCEA bsAb
CD40 mAb
Isotype
%CD40+ CD86+ cDC2 out of Viable CD45+
0.0
0.1
0.2
0.3
CD40xCEA bsAb
CD40 mAb
Isotype
%CD40+ CD86+ cDC1 out of Viable CD45+
0.0
0.2
0.4
0.6
CD40xCEA bsAb
CD40 mAb
Isotype
CD40xCEA bsAb
CD40 mAb
Isotype

Figure 27

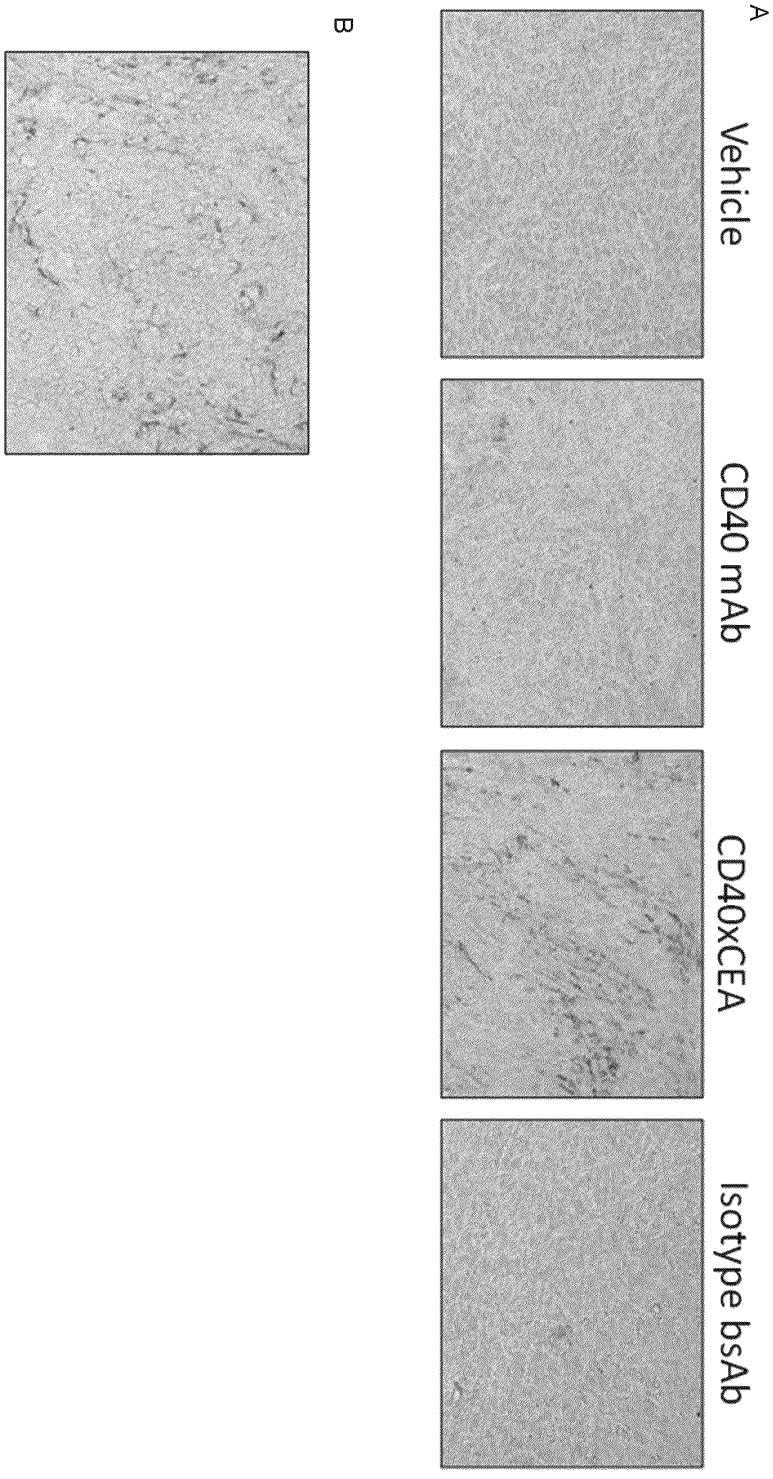
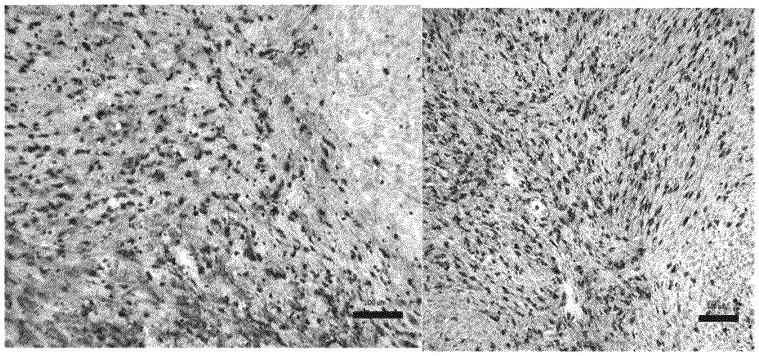


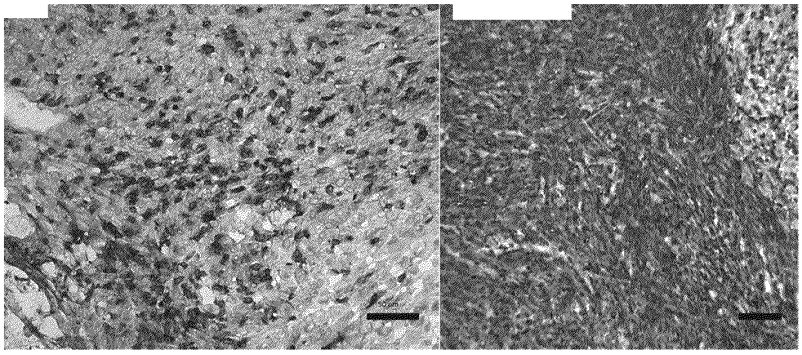
Figure 28 (1/2)

A

CD4 CD8



CD3 CD45



B

	B16, #6	B16, #7	B16, #9	MB49, #2	MB49, #4	MB49, #5	spleen
CD4	0-1+	1+	1-2+	3+	2-3+	3+	3+
CD8	0-1+	0-1+	1+	3+	2-3+	2-3	3+
CD3	0-1+	1+	1-2+	3+	3+	2-3+	3+
CD45	2+	2+	2-3+	4+	4+	4+	4+

Figure 28 (2/2)

C

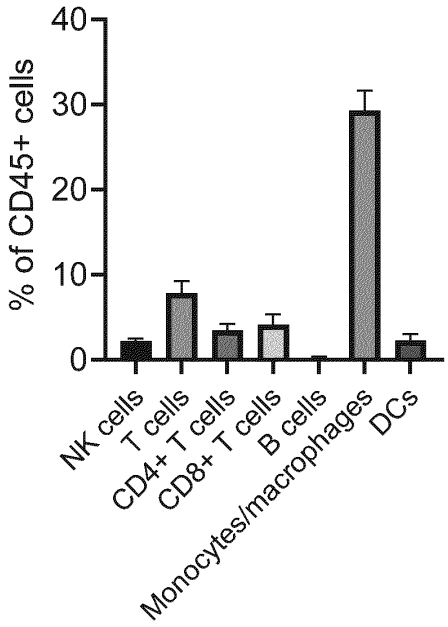


Figure 29 (1/2)

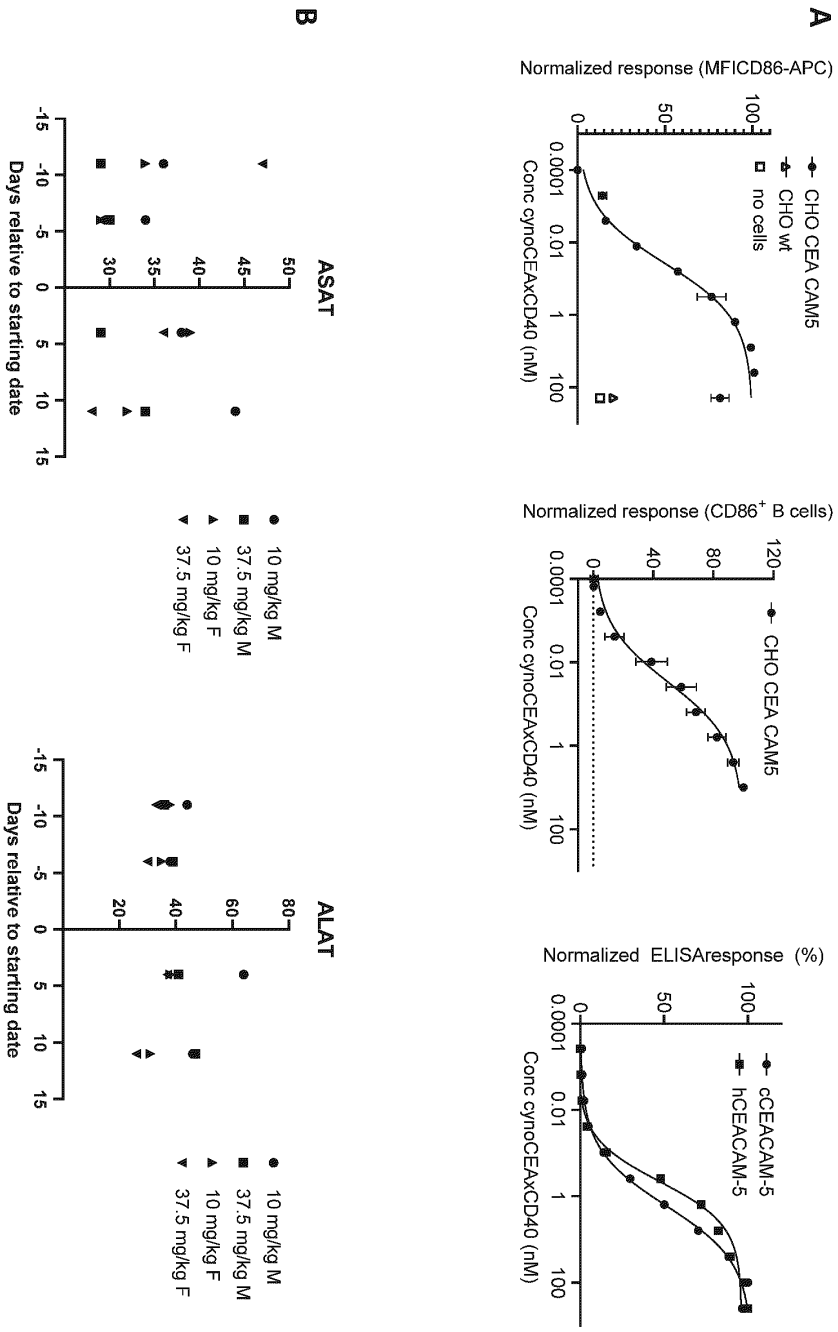

A
Normalized response (MFICD86-APC)
CHO CEA CAM5
CHO wt
no cells
Conc cynoCEAxCD40 (nM)
Normalized response (CD86+ B cells)
CHO CEA CAM5
Conc cynoCEAxCD40 (nM)
Normalized ELISAresponse (%)
cCEACAM-5
hCEACAM-5
Conc cynoCEAxCD40 (nM)
B
ASAT
ALAT
10 mg/kg M
37.5 mg/kg M
10 mg/kg F
37.5 mg/kg F
Days relative to starting date

Figure 29 (2/2)

C

IL-6 (pg/mL)

Dose level	Sex	Day1			Day8		
		0h	4h	24h	0h	4h	24h
10 mg/kg	M	<LLOQ	158	<LLOQ	<LLOQ	<LLOQ	<LLOQ
10 mg/kg	F	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
37.5 mg/kg	M	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
37.5 mg/kg	F	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ

LLOQ = 37.5 pg/mL

TNFa (pg/ml)

Dose level	Sex	Day1			Day8		
		0h	4h	24h	0h	4h	24h
10 mg/kg	M	176	237	<LLOQ	<LLOQ	273	<LLOQ
10 mg/kg	F	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
37.5 mg/kg	M	<LLOQ	111	<LLOQ	<LLOQ	<LLOQ	<LLOQ
37.5 mg/kg	F	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ

LLOQ = 37.5 pg/mL

Figure 30 (1/4)

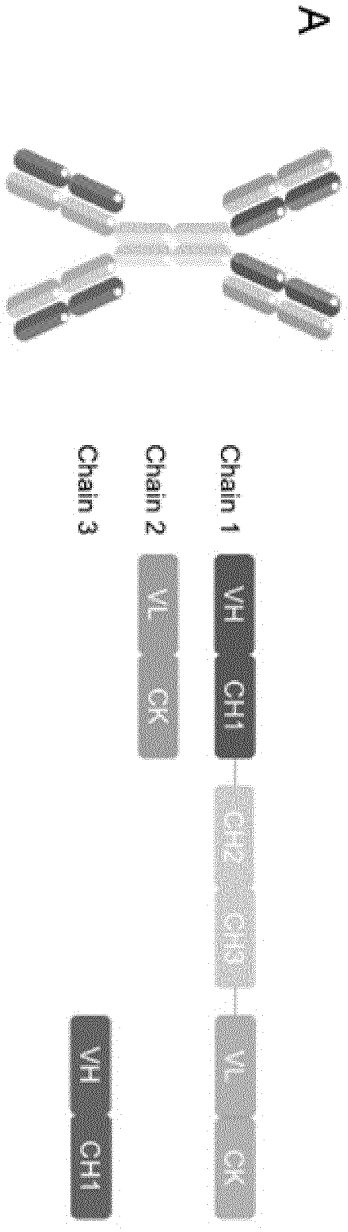


Figure 30 (2/4)

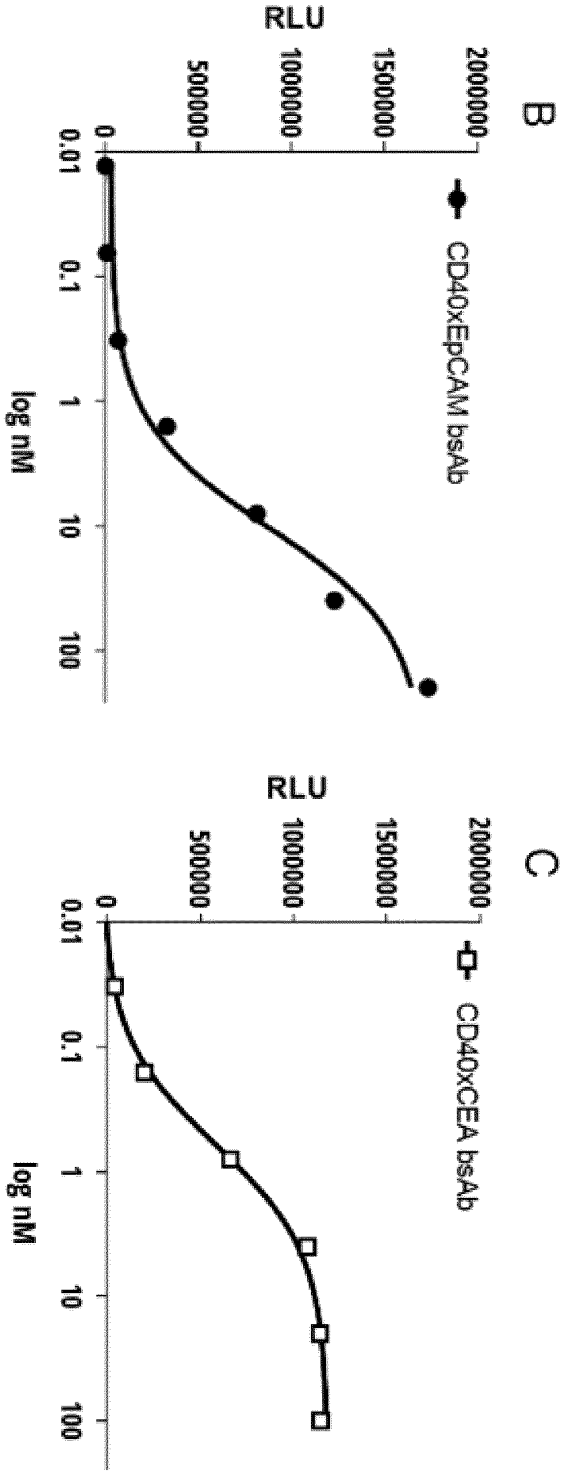

B
RLU
0
500000
1000000
1500000
2000000
0.01
0.1
1
10
100
log nM
CD40xEpCAM bsAb
C
RLU
0
500000
1000000
1500000
2000000
0.01
0.1
1
10
100
log nM
CD40xCEA bsAb

Figure 30 (3/4)

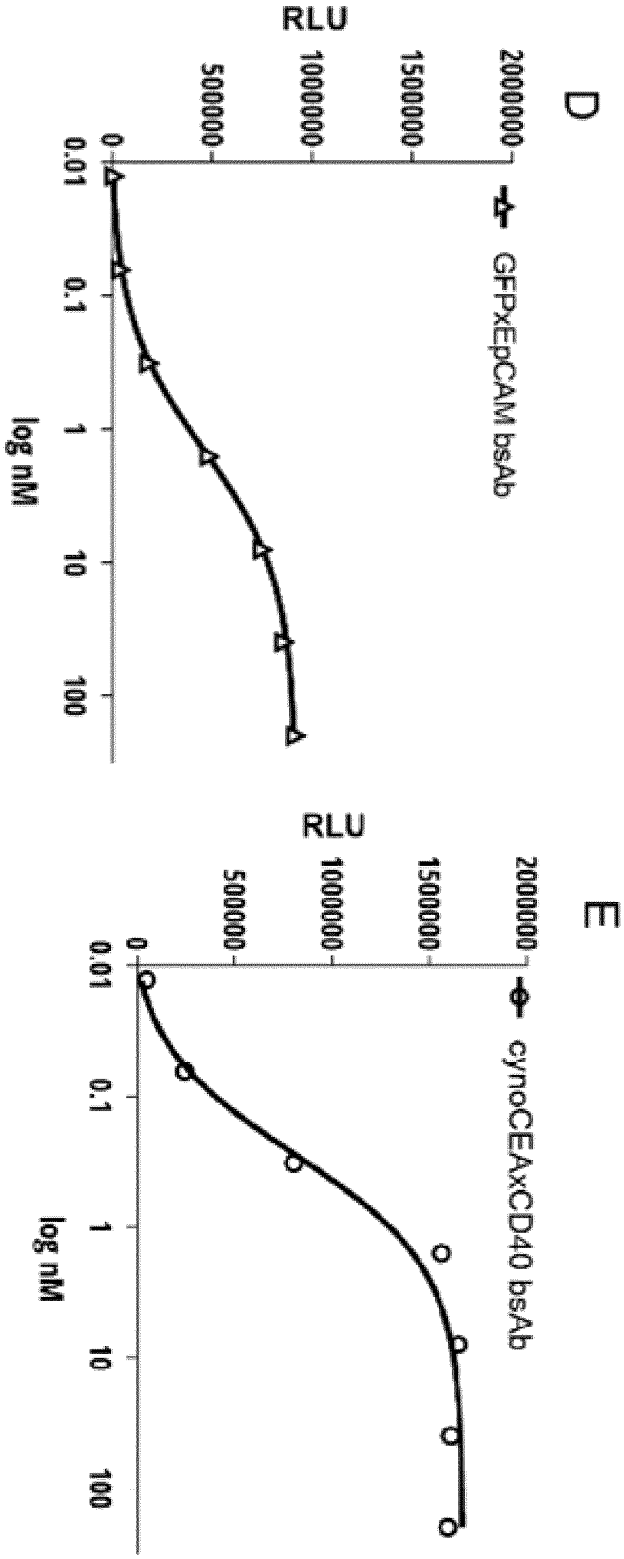

D
RLU
0
500000
1000000
1500000
2000000
GFPxEpCAM bsAb
log nM
0.01
0.1
1
10
100
E
RLU
0
500000
1000000
1500000
2000000
cynoCEAxCD40 bsAb
log nM
0.01
0.1
1
10
100

Figure 30 (4/4)

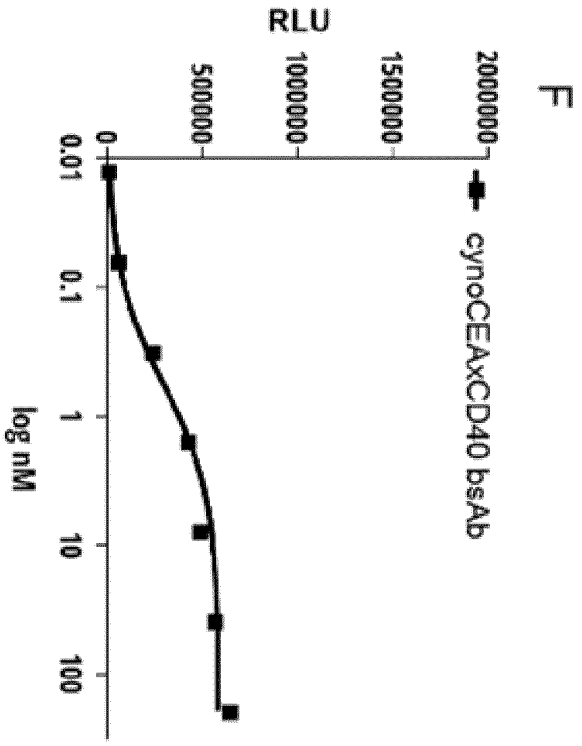

F
RLU
0
500000
1000000
1500000
2000000
cynoCEAxCD40 bsAb
log nM
0.01
0.1
1
10
100

Figure 31

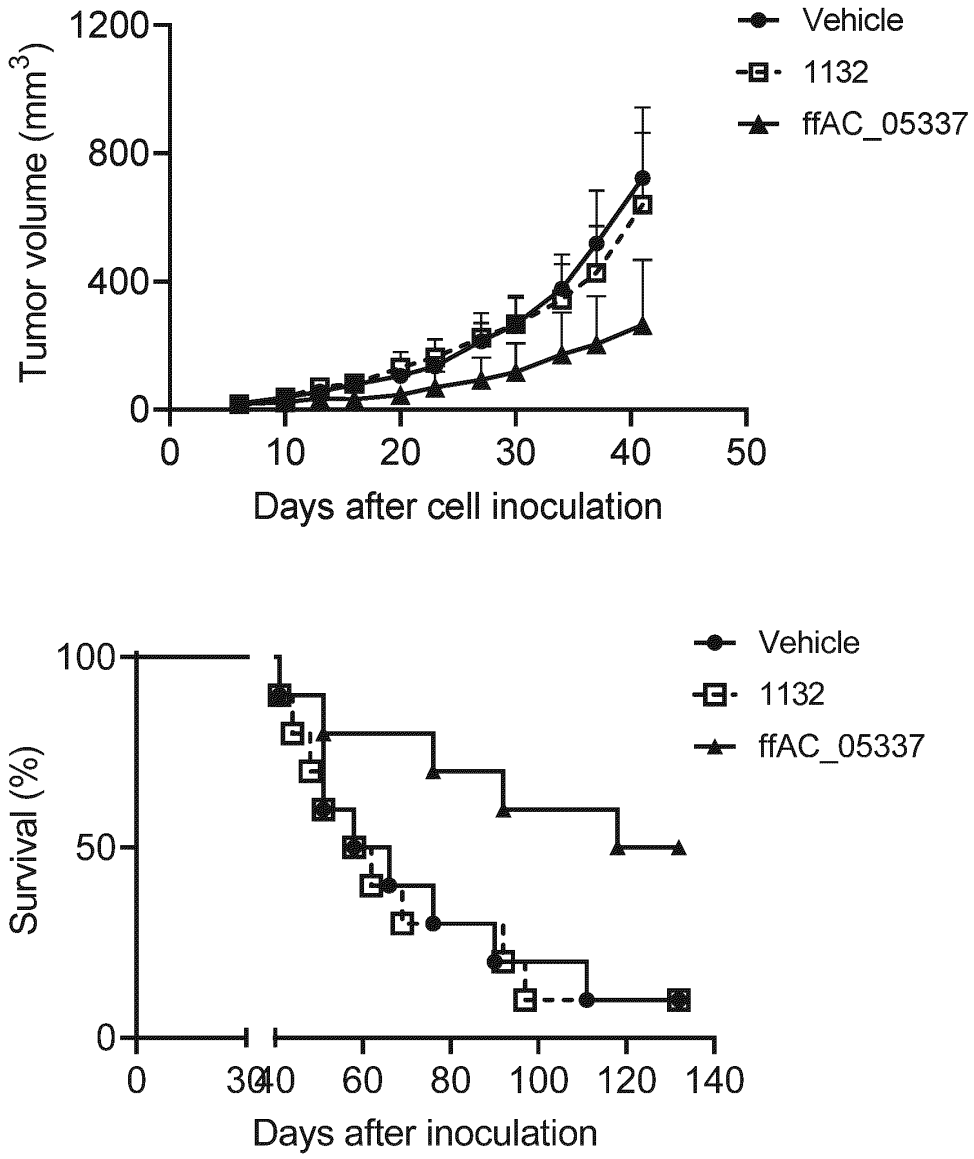

Tumor volume (mm3)
1200
800
400
0
0
10
20
30
40
50
Days after cell inoculation
Vehicle
1132
ffAC_05337
Survival (%)
100
50
0
0
30
40
60
80
100
120
140
Days after inoculation
Vehicle
1132
ffAC_05337

Figure 32 (1/2)

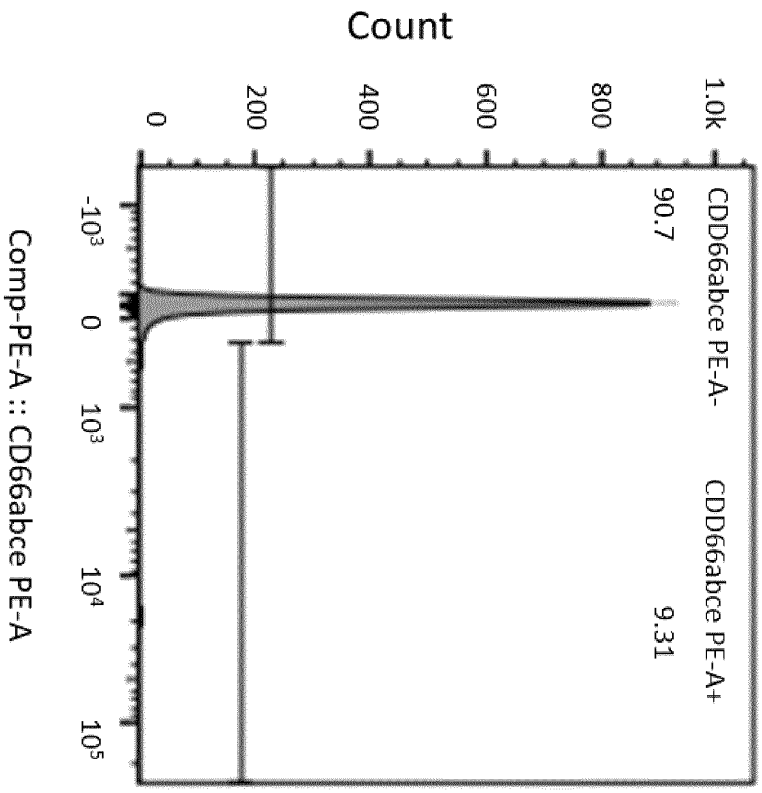

Count
0
200
400
600
800
1.0k
CDD66abce PE-A-
90.7
CDD66abce PE-A+
9.31
Comp-PE-A :: CD66abce PE-A
-10³
0
10³
10⁴
10⁵

Figure 32 (2/2)

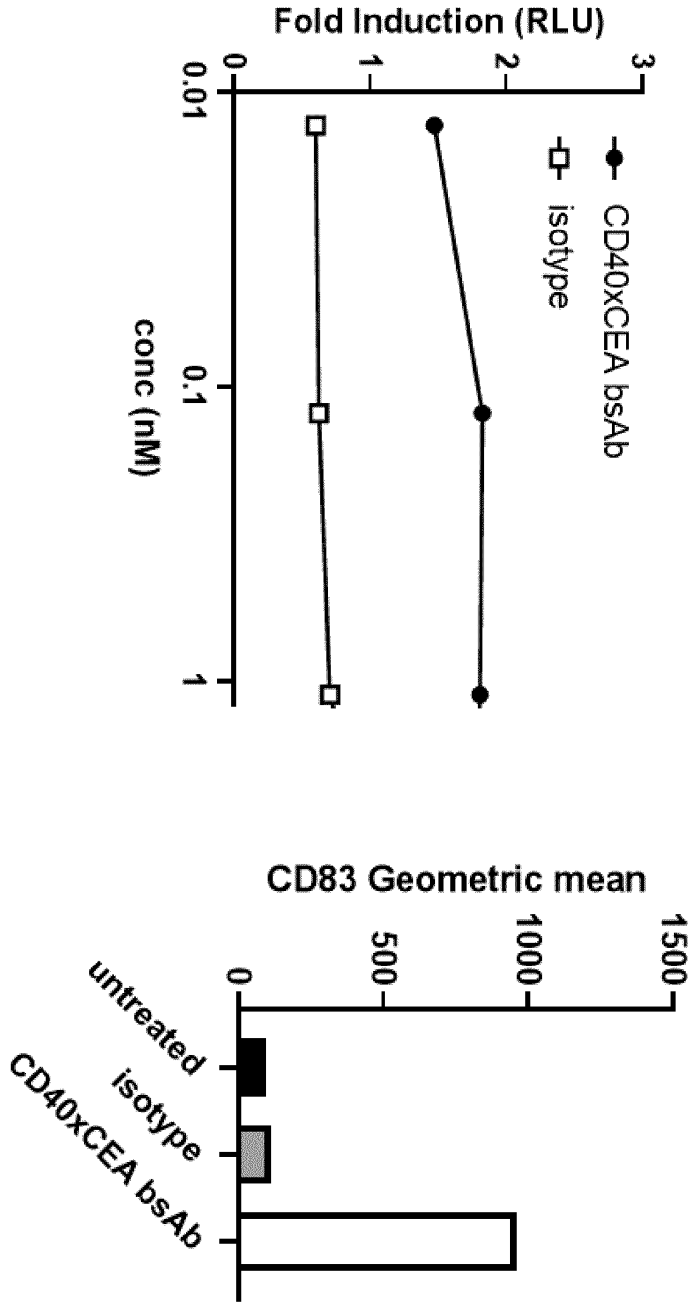

Fold Induction (RLU)
0
1
2
3
0.01
0.1
1
conc (nM)
isotype
CD40xCEA bsAb
CD83 Geometric mean
0
500
1000
1500
untreated
isotype
CD40xCEA bsAb

Figure 33 (1/2)

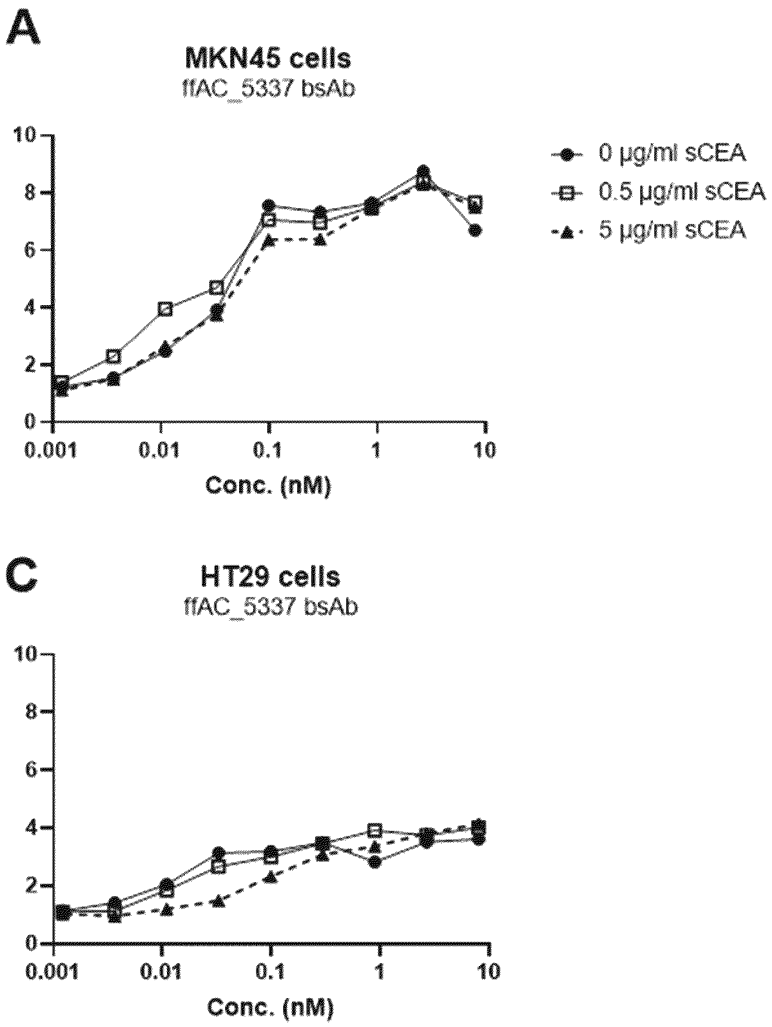

A
MKN45 cells
ffAC_5337 bsAb
0 µg/ml sCEA
0.5 µg/ml sCEA
5 µg/ml sCEA
10
8
6
4
2
0
0.001
0.01
0.1
1
10
Conc. (nM)
C
HT29 cells
ffAC_5337 bsAb
10
8
6
4
2
0
0.001
0.01
0.1
1
10
Conc. (nM)

Figure 33 (2/2)

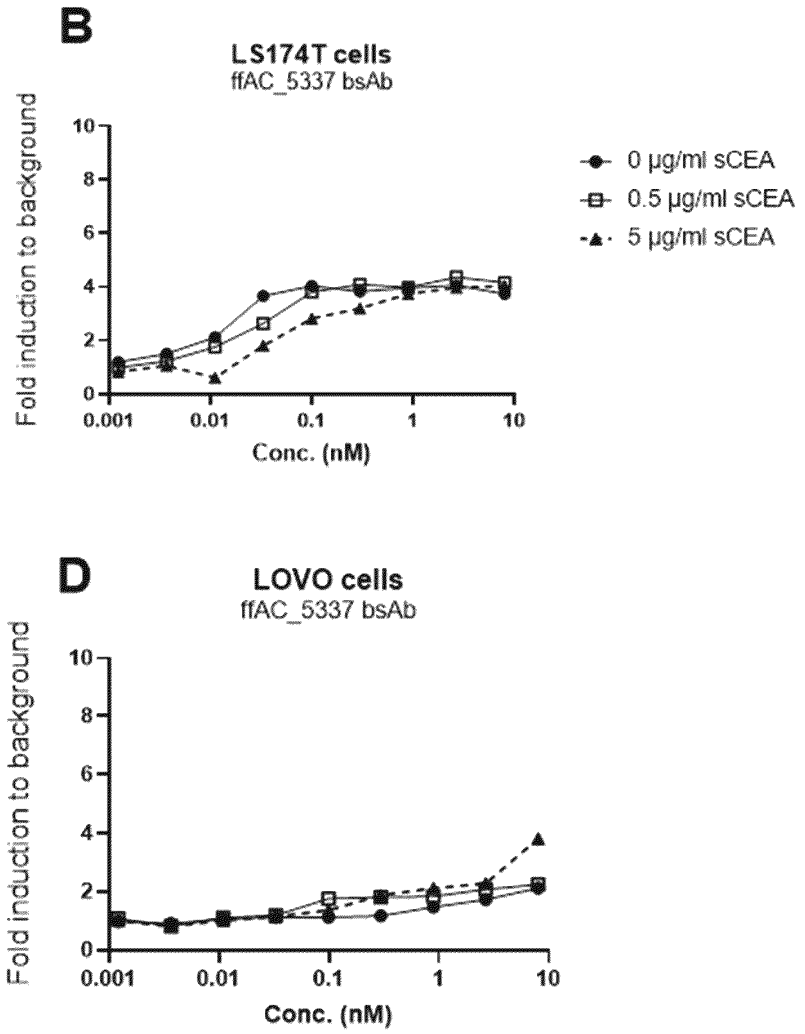
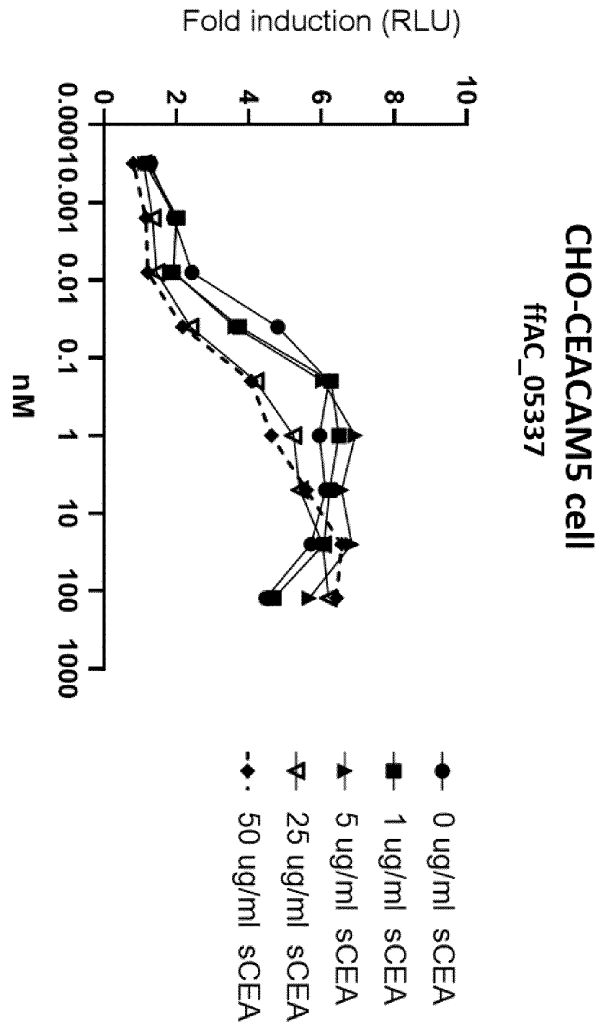

B
LS174T cells
ffAC_5337 bsAb
Fold induction to background
Conc. (nM)
0 µg/ml sCEA
0.5 µg/ml sCEA
5 µg/ml sCEA
D
LOVO cells
ffAC_5337 bsAb
Fold induction to background
Conc. (nM)

Figure 34


Fold induction (RLU)
0
2
4
6
8
10
0.0001
0.001
0.01
0.1
1
10
100
1000
nM
CHO-CEACAM5 cell
ffAC_05337
0 ug/ml sCEA
1 ug/ml sCEA
5 ug/ml sCEA
25 ug/ml sCEA
50 ug/ml sCEA